BRAIN

A JOURNAL OF NEUROLOGY

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A Journal of Neurology

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MARCH, 1939

BRAIN.

PART 1, VOL. 62.

THE CEREBELLUM OF MAN.[1]

BY GORDON HOLMES.

THE unique place that Hughlings Jackson occupies in the history of neurology depends not on descriptions of diseases or syndromes previously unrecognized, but on the methods which he introduced into the clinical study of the nervous system and on the numerous contributions he made to the modes of its activity in health and in disease. He insisted upon accurate observation, on a careful and systematic analysis of the facts observed into their simplest components, and a study of the latter for the light they may throw on the normal functions of the organ which is affected. As the cerebellum repeatedly claimed Jackson's interest a study of its functions by the methods he taught is an appropriate subject for a lecture devoted to his memory.

My aim in this study will be to review facts or observations which have been acquired since my previous contributions to the symptomatology of cerebellar lesions (Holmes 1917-1922), to reinterpret where necessary earlier observations, and to discuss their physiological significance. During these sixteen years numerous clinical observations have been published and an enormous amount of experimental work has been devoted to the cerebellum, but the conclusions drawn from them are so discordant that it seems wiser to omit reference to them when possible and to attempt an independent study of the symptoms which result from lesions of it in man, describing them as simply and unequivocally as possible without the use of the conventional terms which have undoubtedly confused the subject.

The divergencies between the observations of those who have studied experimental animals is particularly confusing; for instance, numerous

[1] The tenth Hughlings Jackson Memorial Lecture delivered before the Section of Neurology, Royal Society of Medicine, on December 16, 1938.

physiologists as Rademaker, Dusser de Barenne and others have failed to find many of the symptoms with which the clinician is familiar, and even within the last year Keller, Roy and Chase have concluded that in dogs, and even in monkeys, the neocerebellum, which includes the greater part of the organ in man, is not essential for any of the functions which have been attributed to it. Other physiologists, however, as Bremer and Fulton and his collaborators, have recently described disorders similar to those which the clinician sees. The discrepancies are largely owing to the animals used in the experiments, for in the carnivora removal of the cerebellum causes few characteristic disorders, and even in the monkeys the symptoms are not pronounced and often transient; it is only in the apes that, to use Fulton's words, "conspicuous and enduring" symptoms occur. It is therefore obvious that the activity of the cerebellum is more essential in the higher steps of the phylogenetic ladder, and a physiological study in man may consequently provide more valuable information on its functions. Further, as Walshe (1927) and others have emphasized, the disorders which result from destructive lesions are seen mainly in voluntary movements, a greater range and variety of which can be investigated in man than in lower animals.

Hypotonia.

Diminution of muscular tone is now generally recognized as one of the fundamental symptoms of acute cerebellar injuries in man, but it is less apparent or less easy to detect in chronic or long standing disease and in some of the systemic degenerations. It has been denied that hypotonia occurs in lower animals after extirpation of the cerebellum, but Bremer has recognized it in the cat and dog, and Fulton and Dow described it as "conspicuous and enduring" after even small lesions of the neocerebellar cortex in apes.

A clear definition of what is in this connection meant by tone is essential as the term has been often applied by physiologists and clinicians to different states of muscle. To the clinician tone generally means the constant slight tension characteristic of healthy muscle, which offers a steadily maintained resistance to stretching; it is recognized by the resistance experienced when the limbs are moved or displaced passively. Sherrington describes tone as a steady contraction of muscles dependent on the activity of spinal reflexes but modifiable by supra-segmental mechanisms, the function of which is maintenance of posture and postural adaptation. Owing to its plasticity the tension of normal muscle is immediately adjusted to changing conditions and remains constant regardless of its length. It is

in this sense the term is employed here. A lack of tone can often be recognized by handling the limb, but the essential fact is that the hypotonic limb can be displaced with unnatural ease from any position determined by contraction of its muscles; its posture is not adequately fixed by their tonic contractions.

The presence of hypotonia in cerebellar disease can be demonstrated by many clinical tests, but as confusion still exists as to what is denoted by the term in modern neurology a few instances may be given. If, for instance, the outstretched arms rest lightly on a bar the normal limb keeps its position or sags but little when the bar is suddenly removed, but the hypotonic

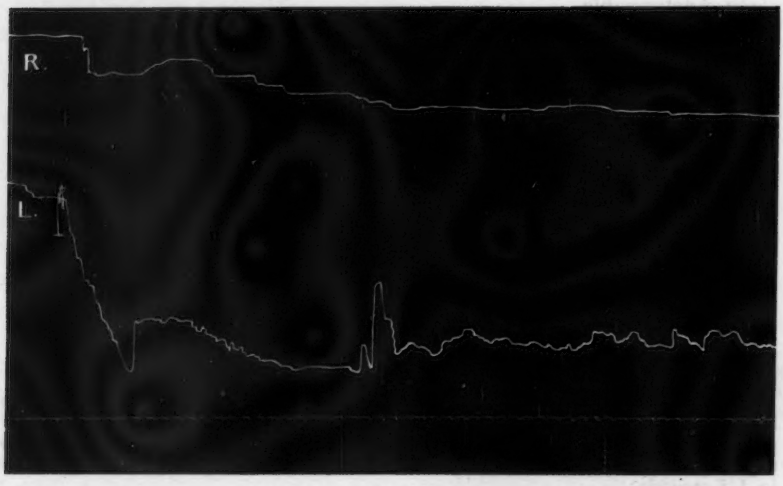

FIG. 1.—A support was suddenly withdrawn from the two outstretched arms of a man with a lesion of the left side of the cerebellum. The left (affected) arm fell at once through a larger angle and developed an irregular tremor. The time marker records seconds.

arm falls through a greater angle and may fail to maintain its new posture (fig. 1). This is more striking if the hand carries even a moderate weight; when its support is released it falls more abruptly, sways about and regains stability slowly, and irregular contractions can be seen or felt in the muscles that should hold it up (fig. 2). The leg in like manner falls heavily and inertly to the bed when it is suddenly unsupported. When the arms are extended horizontally the affected limb is more easily displaced by a tap on the wrist; it gives at the shoulder and frequently flexes or extends passively at the elbow. When shaken the distal segments of the limbs swing more passively and through a greater range. Similarly, if while the

patient stands erect he is rotated or otherwise moved the hypotonic arm swings more freely. If while a normal person is lying supine a leg is suddenly jerked upwards by a hand under the thigh, the heel rises from the bed since the tone of the quadriceps extensor tends to keep the knee extended, but in the hypotonic limb the knee flexes at once and the heel merely drags along the bed or floor.

It is true that the patient may succeed for a time in maintaining a posture by contracting voluntarily the muscles acting on the joint or joints concerned, but the limb soon becomes tremulous and the effort tires; on the other hand a limb in which posture depends mainly on tone is relatively indefatigable.

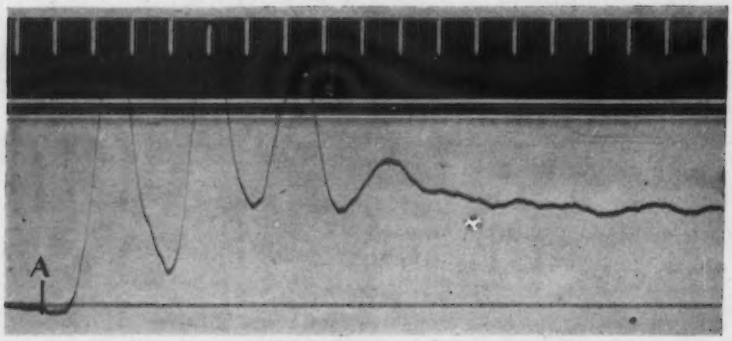

FIG. 2.—A tracing obtained by a tambour placed over the biceps muscle. The hand carried a weight of 2 pounds; at A a support on which it rested was suddenly removed. The tracing shows the irregular contractions of the muscle when it was exposed to the sudden strain, and its delay in acquiring even relative stability. Time in 1/5 seconds.

These examples illustrate the effects of diminished postural tone which alone, or by reinforcing voluntary effort, tends to fix each part of the body in the attitude which it occupies, and they show that volitional contraction of the muscles alone is not adequate to maintain posture.

But tone plays an equally important part in movement, which can be regarded in Jackson's words as a succession of postures; it co-operates with the phasic contractions of the muscles and by virtue of its plasticity assures the appropriate attitudes of the moving segments, as well as the postures of the parts on which they move. It may be that in long-standing disease of the cerebellum and in such slowly progressive affections as the systemic degenerations, the muscles regain through the activity of other parts of the nervous system some capacity to fix attitudes and to resist stretch so that

hypotonia is not so easily recognized on clinical examination, but the more complex function of adapting tone to changing posture during movement remains defective and contributes to the disturbances included in the term "ataxia."

When one side of the cerebellum alone is injured the hypotonia, like the other motor disorders, is restricted to the muscles of the same side of the body, and it appears that no matter how small the lesion may be all the muscles of this side are hypotonic. It is usually more easily demonstrated in the arm than in the leg, and is more pronounced in the proximal muscles which are normally more concerned in the determination of postures.

The fact that the knee-jerk and other stretch reflexes can be elicited has

FIG. 3.—Tracings from a pendular knee-jerk. A records the displacement of the leg and its first oscillation after the jerk: B, a tracing obtained by a tambour placed on the quadriceps muscle. In the latter no after-contraction is visible. Time by a tuning fork of 128 vibrations per second. Read from right to left.

been an argument against the existence of hypotonia (Sager), but though the cerebellum may augment muscular tone the absence of this function does not abolish the spinal reflexes. In the presence of an acute cerebellar lesion the stretch reflexes may, however, be modified. Frequently the knee-jerk is not so easily obtained, or the response to a tap on the patellar tendon may be variable, or the excursion of the leg may be excessive. The character of the jerk may be altered too, since owing to the absence of a "shortening reaction," or tonic contraction supervening on the initial contraction of the quadriceps, the momentum of the falling leg is unchecked and it swings like a pendulum, as it would if it were merely hinged at the knee (fig. 3). Sherrington (1915) has in fact emphasized that the knee-jerk is not a postural reaction and is therefore not a direct sign of tone, but the "shortening reaction" appended to the jerk contraction is, and he has

described characteristic pendular jerks in states in which the reflex excitability of postural tone was low. The pendular knee-jerk of cerebellar disease is consequently evidence of diminished postural tone. It is also an illustration of the influence which the cerebellum may exert on primitive spinal activities.

When in a limb possessing normal muscular tone the patellar tendon is struck, an immediately following contraction of the hamstrings can be readily felt by fingers placed behind the knee; like the quadriceps, these muscles respond to the sudden increase of tension in them due to extension of the leg. This is often absent on the side of a cerebellar lesion; in the flexors of the knee as in the extensors there is a less regular reaction to stretch, and its absence increases the tendency to passive oscillation of the leg.

There are other phenomena associated with, and probably related to, the tonelessness of the muscles and their failure to respond readily to sudden elongation. When, for instance, a normal elbow is flexed strongly against resistance and the resistance is suddenly released the excursion of the movement is quickly checked, but the toneless forearm flexes till arrested mechanically. Similarly, when the arm is relaxed the hand can be flung into the patient's face with so much force as to hurt him; even when repeated several times the patient fails to arrest his limb, or prevents his hand striking his face only by diverting it to another direction. That this is not simply due to a failure of voluntary effort to arrest the moving hand is shown by the fact that in a spastic limb, in which voluntary control as well as the cortical reflexes are defective, the movement is checked at once, and the elbow may be extended by an abrupt contraction of its extensors in response to a sudden increase of tension in them.

Similar phenomena can be observed in the lower limbs. When relaxed the leg can be thrown to the bed, or to the floor, or against the other limb with such momentum as actually to hurt the patient.

From these observations it is obvious that the hypotonic muscles do not respond by contraction to a stretch suddenly imposed on them so readily as the normal.

The abnormal attitudes frequently observed can be also explained by the hypotonic state of the muscles. If a unilateral cerebellar lesion is present the ipsilateral shoulder often droops, the arm hangs fully extended by the side and the limbs may lie in any position to which gravity has brought them. Several observers have recognized that in man and animals attitudes which would normally cause discomfort are less promptly corrected, and some, as Lewandowsky, Goldstein and Dusser de Barenne

(1937), have interpreted this as due to sensory defects or to disturbances in the afferent paths. From numerous examinations I have no doubt, however, that in man even extensive lesions of the cerebellum involve no form of conscious sensation. In the normal limb the discomfort of an unnatural attitude is due mainly to tension in the overstretched muscles; owing to diminished elasticity of the hypotonic muscles their intrinsic receptors are not excited by the same degree of elongation.

The instability of a limb and the irregular tremor which develops in it during attempts to maintain attitudes against gravity and mechanical forces are evidently due to defective postural fixation and to voluntary corrections of its deviations. Sherrington (1915) has shown that at lower levels of the nervous system postural tone fuses with muscular contractions otherwise excited and makes them more continuous and sustained. A failure of postural tone to reinforce voluntary attitudes is obviously one of the causes of such tremor, which is consequently related to hypotonia. It is doubtful if fatigability, which is a feature of the hypotonic limbs, is an important factor, or if asthenia of the muscles plays a part, as the limb may become tremulous as soon as it is unsupported (fig. 1).

Occasionally a more regular and rhythmical tremor occurs, probably when the superior peduncles are injured; Ferrier and Turner originally described such tremor after section of these peduncles, and this has been confirmed by Walker and Botterell and by Fulton and Dow in primates.

Rigidity or a hypertonia of muscles has been described by several workers after ablation of the palæocerebellum (Rademaker, Sager), and Hughlings Jackson (1890) described tonic seizures in patients with lesion of the vermis. In man, however, the palæocerebellum is represented by a relatively small part of the organ, and it can be rarely involved alone by local lesions. I have no definite observations that muscular tone is ever increased in cerebellar disease, but I have seen a few cases of anterior and mesial lesions in which the characteristic disorders of movement were not accompanied by a definite diminution of tone.

Asthenia and Fatigability.

Since Luciani originally described asthenia, or paresis of movement, as one of the fundamental features of destructive lesions of the cerebellum there has been much dispute as to whether muscular power is ever affected. Most of those who have undertaken animal experiments have failed to confirm Luciani's statement, but Bremer, Rossi and Simonelli, and Fulton and Dow observed evidences of feebleness in animals soon after operation. Goldstein has described it in man, and measurements which I have

published place beyond doubt that it occurs (Holmes, 1917). In acute lesions strength may be reduced to half that of the normal limb, but though asthenia may persist for months it diminishes gradually or becomes less apparent. The following figures represent the averages of several measurements obtained from two patients with gunshot wounds of one side of the cerebellum. In one the measurements were made nearly ten weeks after the wound was inflicted.

	Case 1 (thirty days).		Case 2 (sixty-eight days).	
	Unaffected Side (R)	Affected Side (L)	Unaffected Side (R)	Affected Side (L)
Grasp	12·4	5·8	17	10
Flexion of Elbow ...	26·2	15·3	10	7
Extension of Elbow ...	11·8	5·2	7	4·6
Supination	10	5·2	—	—
Pronation	20	14·5	—	—
Depression of Arm ...	—	—	10·4	6·5
Flexion of Ankle ...	—	—	12·5	10·5
Extension of Ankle ...	17	15	18	15
Depression of Leg ...	—	—	10·5	9

This feebleness is often recognized by patients; many complain that the arm particularly "feels weak and heavy," "I have to put more effort into it to move it," "I can't put force into it," "I can't lift the same weight with it." It is usually greater in the proximal segments of the limbs, and in the arm than in the leg. There is often associated with it an obvious reluctance on the part of the patient to move the affected limbs, especially in gestures and spontaneous actions. Although always greater in hypotonic limbs there is no evidence that asthenia is due to disturbance of tone, and as it can be demonstrated in even the simplest actions it cannot be attributed to defective co-operation of muscle groups or to disorders of movement. It must therefore be regarded as a primary or fundamental symptom.

A tendency of the affected limbs to tire more readily than the normal has been generally recognized; Botterell and Fulton have described it in apes. It seems to be closely related to the degree of asthenia which is present.

Disorders of Voluntary Movement.

But the most prominent disturbances of function that result from destructive lesions of the cerebellum are disorders of voluntary movement. These disorders are usually described under such terms as "ataxia," "incoordination" and "asynergia," but to avoid confusion to which they have given rise they will be employed here as little as possible.

In dealing with these disorders of movement it is important to recall

Hughlings Jackson's teaching. He insisted "It will not suffice to speak of co-ordination as a separate faculty, co-ordination is the function of the whole and of every part of the nervous system" (1870). And he repeatedly pointed out that there are two factors in the causation of irregularity of movement: "Half of the symptomatology of disorders of co-ordination with negative central lesions is paralysis (i.e. loss of function) owing to that negative central lesion. But the other half is from forcing of other movements by overactivity of perfectly healthy nervous arrangements." . . .

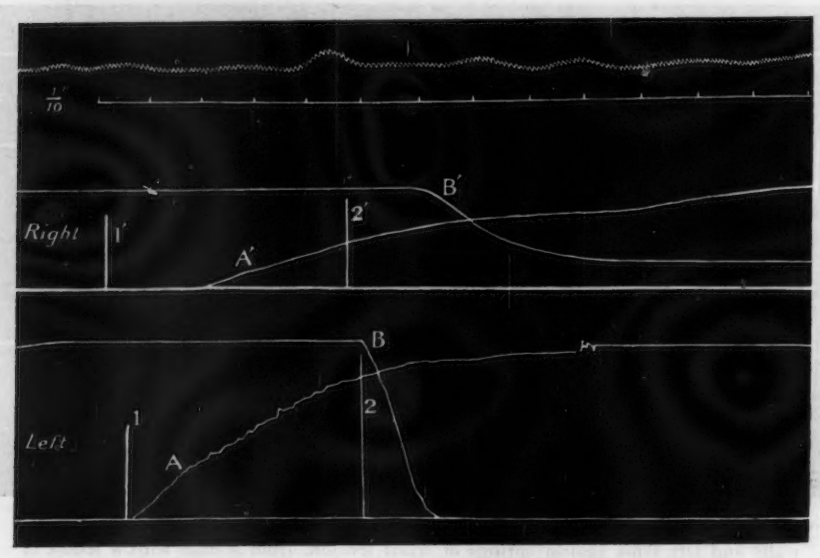

FIG. 4.—From a case of injury to the right lateral lobe. The patient was asked to grasp simultaneously with his two hands against two springs of equal strength. 1 and 1^1 represent the simultaneous ordinates, A and A^1 the lines traced on a rapidly revolving drum. The drum was allowed to complete one revolution and a signal to relax was then given; 2 and 2^1 represent the simultaneous ordinates, and B and B^1 the tracings of relaxation. Time by a tuning fork of 128 vibrations per second. (Holmes, 1917.)

"The two elements, negative and positive, constitute the disorder of co-ordination" (1888).

An attempt to resolve these disorders into their simplest factors can be most profitably undertaken by studying first simple movements, that is movements at one joint and in one direction only, the rest of the limb being fixed, as flexion or extension of a single finger, or of the elbow or

knee. One of the great disadvantages which clinical investigations suffer is difficulty in recording and measuring observations accurately by such methods as physiologists employ. Tracings of simple movements can be obtained on a revolving drum, but the most satisfactory method of recording more complex movements is to attach to the moving part a small electric bulb which is made to flash at rapid but regular intervals by a tuning fork interposed in the circuit and photographing the flashes on the plates of a stereoscopic camera in a darkened room. By this means a

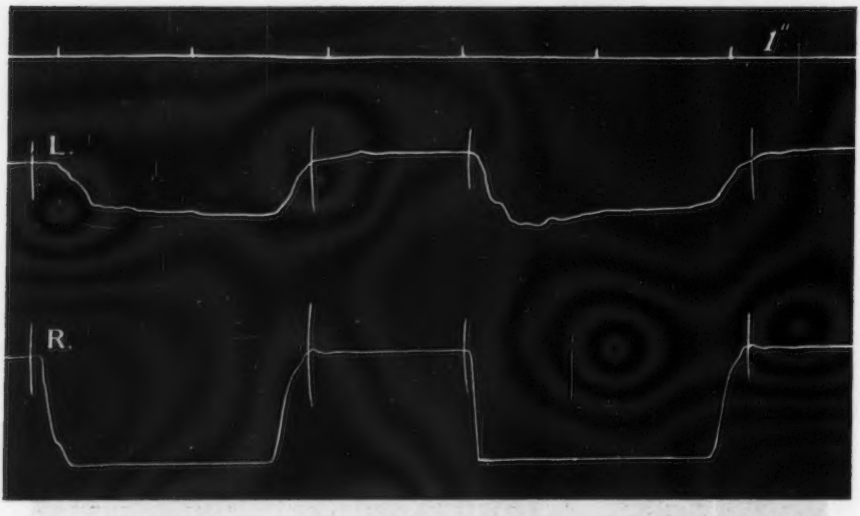

FIG. 5.—Tracings on a slowly rotating drum of simultaneous depression of the right and left arms against springs of equal tension, from a man with a lesion of the left side of the cerebellum. The tracings show delay in starting and slowness in effecting the movements, reduced and irregular exertion of power, and slowness in relaxation on the affected side. Time in seconds.

permanent record of the rate of the movement and of its direction in all three planes of space is obtained (see fig. 7).

Simple movements.—If a simple movement is studied, as flexion or extension of a single finger, or of the forearm at the elbow, while the rest of the limb is supported or fixed, the most prominent abnormalities are due to disturbances in its rate. In the first place there is frequently a delay or slowness in starting motion. This is more readily seen in unilateral lesions when the patient is requested to execute the same movement with the two limbs at a given signal, as to grasp an object simultaneously with his two hands, or to flex or extend his fingers to order (fig. 4). As I have

previously pointed out (1917), the slowness in initiating a movement is generally more pronounced when the patient is not immediately prepared for the signal and in the ordinary activities of the limb, but it is usually apparent even after repeated examinations and when he is aware of the purpose of the test. It occurs equally in unrestricted and in opposed movements. In cases of mild disturbance this delay in initiation may be detected only when tracings of symmetrical movements are taken on a rapidly rotating drum, but it is usually visible or can be felt by fingers placed on the moving part. Goldstein, Bremer and other clinicians have also observed this phenomenon, and Fulton and Dow have described "a conspicuous slowness in initiation of movement" in the chimpanzee. Risien Russell, in experiments on monkeys, was also impressed by the tardy withdrawal of the affected limbs from noxious stimuli. It is usually present in all movements of the limbs, but is often more pronounced at the proximal joints, that is in segments moved by the larger muscles (fig. 5).

Not only are movements initiated more slowly but they usually attain

FIG. 6.—A patient with a right-sided cerebellar lesion was requested to flex and extend each index finger at a slow and uniform rate. The separate tracings were obtained on successive rotations of the drum. The jerky and tremulous character of the movements of the right finger contrasts with the regular and uniform rate of those of the left. Time in seconds.

their ordinary velocity and force more tardily than in the normal limb. This is more obvious if the movement is performed against a resistance, as compressing a dynamometer or pulling against a spring. Under these conditions it may be often seen that the exertion of force is also jerky or intermittent in contrast with the rapidly and steadily increasing power developed by the normal limb (fig. 5).

An equally important though less recognized disorder in all movements, but particularly in those executed slowly and deliberately, is a lack of uniformity in their velocity. Within even short intervals their speed varies, being sometimes slower, sometimes faster than in the normal limb; the natural rhythm and regularity of motion is lost (fig. 6). This can be

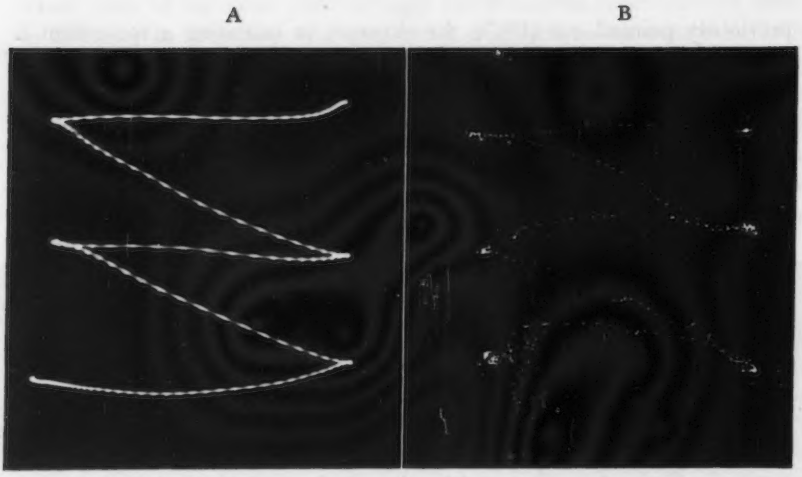

FIG. 7.—Records obtained by photographing points of light attached to the tips of the forefingers as a patient with a lesion of the right side of the cerebellum attempted to move each finger slowly and accurately between series of luminous red points (not visible in the photographs) in a dark room. Each flash of light corresponds to 0·04 second. The range of each movement was about 75 cm. A is the record obtained from the left hand, B, that from the right. The irregularity in the rate and in the directions of movements of the affected hand, and the failure to arrest this finger accurately at the points, are well shown in B.

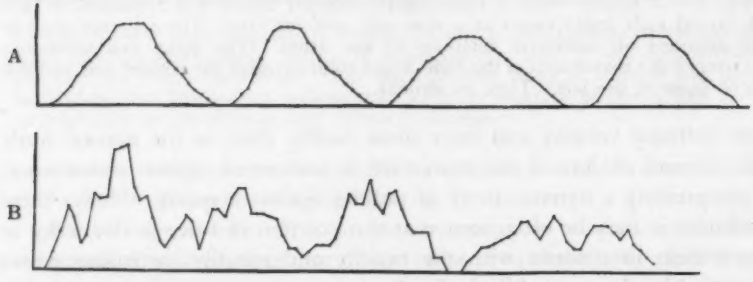

FIG. 8.—An analysis of four of the separate movements of each record in fig. 7, A and B, to show irregularity in the velocity of motion of the right hand (lower curve). The horizontal distance between each dot corresponds to 0·04 second; the heights above the base lines represent the spaces between successive flashes of light and therefore the rate of movement at the corresponding points in space. In three of the excursions of the affected limb he failed to bring the finger to rest on reaching the point to be touched (lower curve).

particularly well demonstrated by analysis of light records, as when this method is employed there is no mechanical restraint to steady the movement (figs. 7 and 8), but it can be also recognized in resisted movements in which the exertion and maintenance of power is jerky and discontinuous (fig. 9). The irregular velocity of movement may appear as an obvious tremor, but the variations in rate are frequently so rapid and small that they can be recognized by graphic methods only.

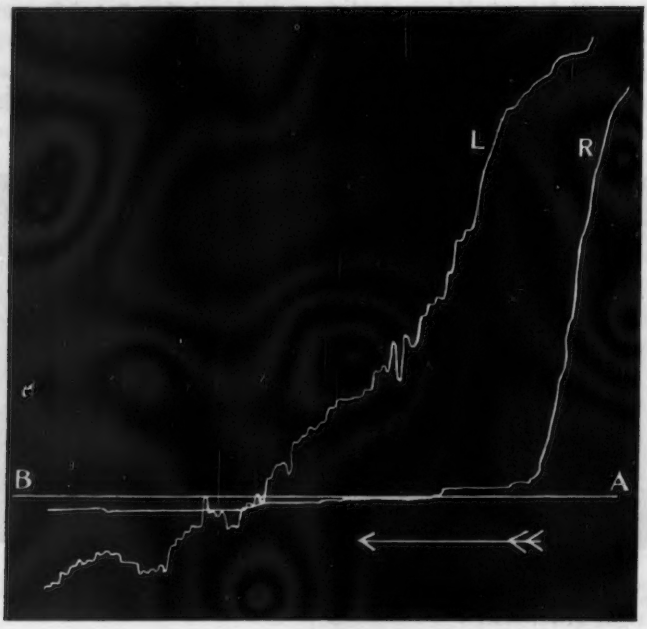

FIG. 9.—The patient, who had a wound of the left side of his cerebellum, was asked to extend springs of equal strength with his two arms on a signal and to maintain the stretch at a level indicated by the line A, B. Note the slowness of the left arm in exerting power, the irregular tremulous character of the movement and the failure to maintain the final posture. Read from right to left.

When one side only of the cerebellum is injured the whole range of movement of the ipsilateral limbs in both man and apes (Fulton and Aring) is often slower and more deliberate than of the normal, but if the limbs are uncontrolled they may attain a greater speed (fig. 10B); the arm or leg may be flung out with unnatural force and velocity, and the hand may swoop down on, or snatch at, any other it wishes to reach. This is

particularly seen in movements with gravity, or when a restraining force is suddenly removed.

In such simple movements there is rarely any pronounced deviation from the direct line provided the proximal segments of the limb are supported or fixed.

The most obvious errors are, however, seen towards the end of movement. As a normal limb approaches its object its velocity declines at a uniform rate till it comes to rest, but the speed of the affected limb is often unchecked till the object is reached or even passed (figs. 7 and 8), and then the error is corrected by a series of jerky secondary movements, or the finger or toe may swing around the point to be touched without actually coming to rest (fig. 10). This excessive range of movement, to which the

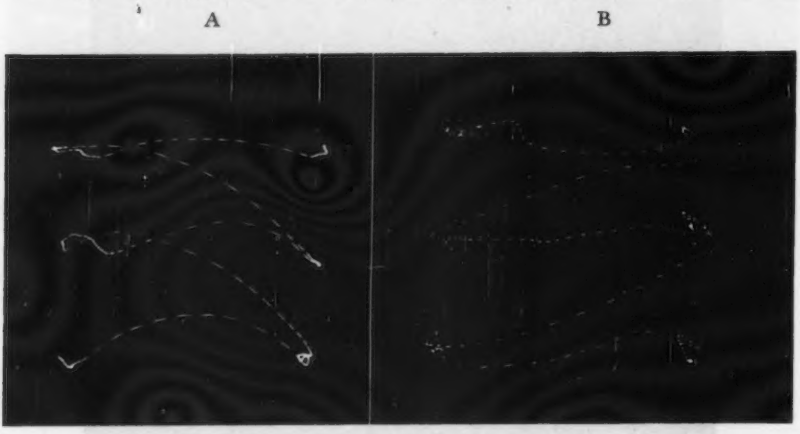

FIG. 10.—Light records as in fig. 7. A is a record obtained from a patient with a lesion of the left side of the cerebellum; B, from another patient with an injury of the right lateral lobe.

term "hypermetria" has been applied, has attracted much attention and has been regarded as a characteristic feature of "cerebellar ataxia," but it occurs in other hypotonic states.

When movements against resistance are studied by graphic methods it is found that hypermetria is due to delay in starting their arrest and slowness in completing it (figs. 4 and 5). The movement, or rather the contractions of the muscles which effect it, may be continued for a fifth of a second or more after the normal limb has come to rest; a fifth of a second may represent a large part of a simple action. These abnormalities in relaxation are very similar to those at the start of movement. Sometimes the one, sometimes the other are the more prominent.

Frequently, however, the excursion of the limb is arrested too soon and the object is attained by similar correcting movements. This premature arrest is sometimes merely a manifestation of lack of uniformity in the rate of movement, but it seems to be commonly due to a voluntary check; it occurs particularly in patients who have experienced the risk of overshooting the mark.

Tremor, which is sometimes apparent during the whole range of movement, is usually more prominent towards its end; the irregular oscillations in the intended direction result from failure of uniform deceleration, but this is complicated by secondary or correcting jerks when the object has not been accurately reached in the first attempt (fig. 7B).

Delay in starting movement and slowness and irregularity in its acceleration are probably fundamental disturbances; as the latency of atonic muscle is not altered they cannot be attributed to hypotonia. The irregularity in rate and force during movement have been attributed to lack of a steadying influence or grading action of the hypotonic antagonists; this is undoubtedly an important factor in slow and deliberate acts, but as these irregularities may be equally pronounced, or even greater, in movements executed against resistance, in which the antagonists are normally relaxed (fig. 9), this explanation is not adequate. They must be therefore attributed to irregular innervation of the prime movers.

Altenburger has described a variation in the action currents of contracting muscles which he regards as a characteristic and fundamental feature of cerebellar affections. His records show, instead of a normally continuous or rhythmical series of oscillations during contraction, groups of separate oscillations, each representing 6-15 action currents, occurring at more or less regular intervals at a rate of 4 to 5 per second. Such a breaking up of the action currents, indicating a discontinuity in muscular contractions, would correspond with the unevenness in rate and force of movement which can be observed directly and demonstrated graphically, but unfortunately his published records were obtained mainly from cases with mesencephalic lesions (Bindearmläsion) and of disseminated sclerosis in which there occur coarse tremors at rest and during motion which differ in essential respects from the characteristic irregularities of movement of cerebellar ataxia. Dr. Denny-Brown, who kindly recorded the action currents in some of my patients with local lesions of the cerebellum, was unable to confirm Altenburger's findings (fig. 11). When an obvious tremor develops at the end of movement rhythmical or irregular intermissions naturally occurred in the records, but no tendency to a grouping of action currents separated by regular intervals could be observed in any stage of

either free or opposed movement. Frequently, however, a waxing and waning of the intensity of the action currents could be seen when the muscles from which they were obtained were contracting irregularly (fig. 11A).

Errors in range of movement, apart from premature voluntary arrest, are simply manifestations of failure of prompt and uniform deceleration which must be due to a primary disturbance in innervation, but delay in

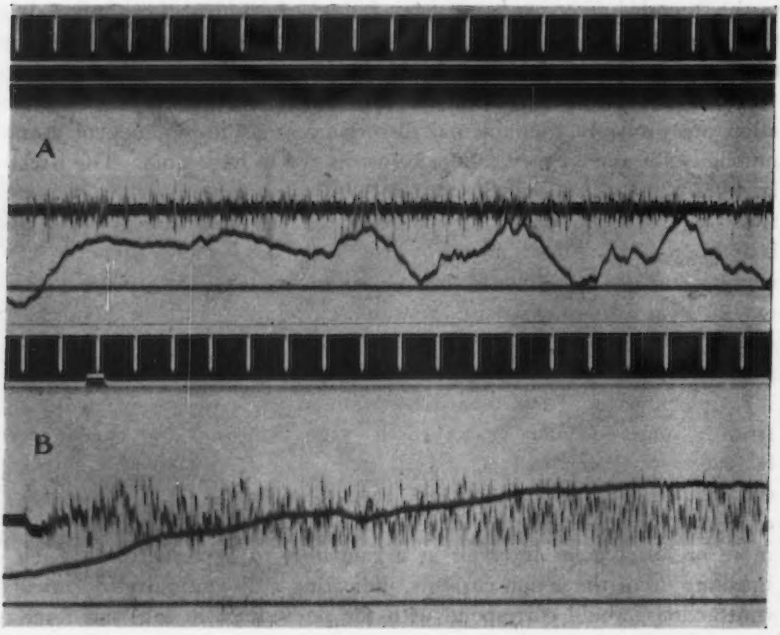

FIG. 11.—Records of action currents from two patients with pronounced cerebellar ataxia. A was obtained from the deltoid during unrestricted abduction of the arm. B obtained from the flexor carpi ulnaris during opposed flexion of the wrist. The unbroken line in each record was obtained by a tambour on the active muscle and represents its contraction.

the intervention of the antagonists to check the movement is certainly another factor. There is no evidence that hypermetria is the direct result of absence of a special "braking" function which the cerebellum exerts in movement (Babinski, Söderbergh, Schilder, Barkman).

These abnormalities of simple movements are generally most pronounced in hypotonic limbs; their relation to hypotonia will be discussed later.

Compound movements.—This term may be applied to movements which involve change of posture at two or more joints, as bringing a finger to the nose, or a heel to the opposite knee. To facilitate description they can be divided into (1) movement in one direction, and (2) movement requiring a change in direction.

In *compound movements in one direction* the irregularities in rate, force and range of each component of the movement complicate the execution of other synchronous or successive components and therefore com-

FIG. 12.—Decomposition of movement. The patient attempted to bring the tip of his finger from a point A above his head to his nose B. He executed the act in two stages; in the first he merely depressed his arm, and in the second stage he brought his finger towards his nose by flexing his elbow. After striking his nose violently the finger was withdrawn and then brought back irregularly. The record was made on a stationary camera plate by a light attached to the tip of the moving finger.

bine as it were in geometric progression so that the error of the whole movement is relatively greater than the sum of those of its parts.

There are, however, other factors in so-called "cerebellar ataxy." In the first place there may be a lack of synchronicity in the separate components of the movement. If, for instance, the patient with a unilateral lesion is requested, when his arm is extended above his head, to bring his index finger to his nose, with his normal limb he does so by simultaneously depressing his elbow and flexing his forearm, so that the tip of the finger follows a more or less straight line from the start to the end of the move-

ment, but on the affected side depression of the elbow is frequently completed before the forearm flexes (fig. 12). When asked to touch a point at arms-length in front of him he often first extends his arm and then swings it about till the finger reaches its aim. Similarly in bringing a heel to the opposite knee the thigh may be bent on the trunk before the knee is adequately flexed, or the knee may flex first. The affected limb "decomposes" the movements in time into its constituent parts, and this naturally leads to errors in direction. Delay in the initiation of one component relative to that of another, and excessive range of one element of the movement, particularly at a proximal joint, are the chief causes of "decomposition," but another factor is the defective fixation of one or other of the moving joints.

Defective postural fixation of the moving limb is also largely responsible for errors in direction of movement which are often a dramatic feature of "ataxia." I have previously drawn attention to its importance (1917) and Noica has described it as the most potent factor in the disorders of movement. Its influence is generally greater at the proximal joints where the weight and momentum of the moving limb particularly require steadying by tonic contraction of the muscles around them. We have seen that when the hypotonic limb is held horizontally outstretched, subject only to the unvarying force of gravity, it soon sags or deviates from its position; such deviations are more likely to occur if posture is complicated by motion of any segment, since the force to which the fixing muscles are exposed varies rapidly with changes in the centre of gravity and in the momentum of the limb. The hypotonic muscles also seem to lack the plasticity by which they can rapidly adapt themselves to changing conditions. The result is that the moving limb is liable to sway about, especially at the shoulder and hip, instead of conforming accurately to the posture or displacement required of it in the action. Finally, lack of a steady or properly adapted base on which to move necessarily interferes with and impairs the accuracy of movement of the more distal segments of the limb.

The influence of deficient postural tone on movement extends to the distal segments of the limbs also. When a patient attempts to bring in succession each finger separately to the tip of his thumb, the thumb frequently fails to keep or to adopt correct postures, and all the fingers tend to flex simultaneously instead of individually, as those which should remain extended are not held in this position by the tone of their extensor muscles. Inability to maintain the correct postural relations of the fingers to one another, to keep those not directly concerned out of the way, is partly responsible for the difficulty in performing delicate actions, as buttoning clothes, striking notes on a keyboard and handling objects.

In movements in which there is a change in direction irregularities are more striking. They may be seen when a finger follows an object which does not keep to a straight line, and when the patient attempts to outline a square or a more complicated pattern it is at the turning points that errors are most pronounced (fig. 13); the overshooting of the aim or the premature arrest of the limb, the attempts at correction, the terminal tremor, and the delayed and irregular start of the next phase, all lead to confusion and

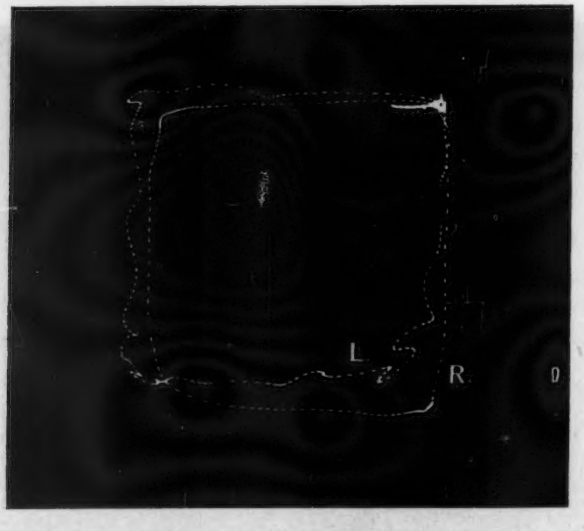

FIG. 13.—Light records of attempts by a man with a lesion of the left side of the cerebellum to outline the square end of a room with the right and left (affected) forefingers in succession. Each flash of light represents the distance covered by the moving finger in 0·04 second.

inaccuracy. Frequently the finger merely sweeps in a curve round the turning point instead of pausing at it.

It is particularly in actions which require reversal of direction that these disturbances are prominent. Babinski, who first recognized the inability of the affected limb to execute alternating movements with normal rapidity and regularity, gave it the name dysdiadochokinesis.

The slower rate and the lack of rhythm depend mainly on time lost at the turn or in reversal; this is partly due to delay in initiating each successive movement, but tracings also show that the individual excursions are usually less rapid than when the normal limb is engaged (fig. 14) but they

may attain a greater velocity (fig. 15). The factors which retard simple movements cannot, however, explain fully the slower rate; it seems probable that a defect in post-inhibitory rebound, which Sherrington (1913) has shown facilitates the transition of one movement to another in the opposite direction, is partly responsible. Since simple segmental reflexes, as the knee-jerk, may be influenced by cerebellar lesions, we may assume that other spinal activities, as post-inhibitory rebound, may suffer too. The fact that the rate, rhythm and range of alternating movements may be improved,

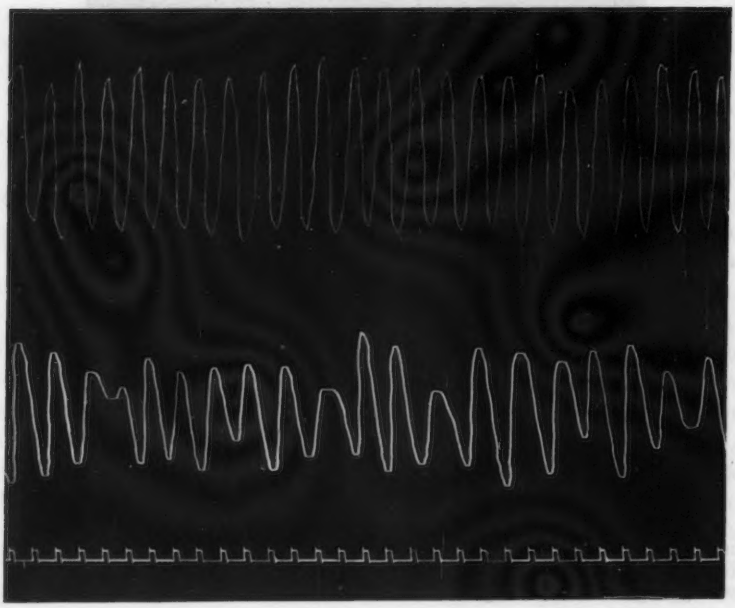

FIG. 14.—Tracings of alternating pronation and supination of the normal (above) and the ataxic arm of a patient with a right-sided lesion of the cerebellum. Time in seconds.

and may even approximate to the normal, when the patient carries a heavy bar in his hand during the pronation-supination test, points to its importance, for the increased momentum of the moving limb increases the tension on the antagonists and excites more readily their succeeding contraction.

The range of the excursions is often irregular too; often excessive when they are not mechanically restricted as in the pronation-supination test (fig. 15), but sometimes less than normal. Failure of prompt arrest of each

movement on the one hand, and its premature arrest on the other, explain these inequalities in range.

But loss of postural tone adds to the difficulties in performing alternating movements. During rapid pronation-supination of the normal forearm the upper arm remains steadily fixed in position, but the affected limb sways about passively and irregularly from the shoulder with the result that the forearm has not a stable base on which to move. This naturally increases the difficulty in moving it rapidly and accurately. Noica has

FIG. 15.—Alternating flexion and extension of the elbow of the normal (L.) and ataxic arm (R.), recorded in succession on a moving camera plate by interrupted lights attached to the index fingers. Each flash corresponds to 0·04 second.

also drawn attention to the important rôle played by defective fixation of the proximal segments in dysdiadochokinesis.

When alternating movements are prolonged, and particularly when the patient is urged to persist in them, the excursions become laboured and forced, the limb tires rapidly and it may eventually come to a standstill as if held up (fig. 16). This is not wholly due to fatigue, for if the limb is handled all its muscles, and not only those actively concerned in the action, may be found rigidly contracted, or the original movement may be replaced or complicated by others. In the pronation-supination test the fingers and wrist may straighten and bend alternately, the forearm may

flex and extend, or the arm may adduct and abduct at the shoulder more or less synchronously with the movements which are desired. Muscular contractions spread aimlessly over the limb. This seems to be a result of excess and confusion of voluntary innervation in the effort to keep up the rhythm of movement when the rate, force and range of the separate excursions and the rapid reversals of direction are not under control. The fact that diversion of attention, as by the simultaneous performance of the

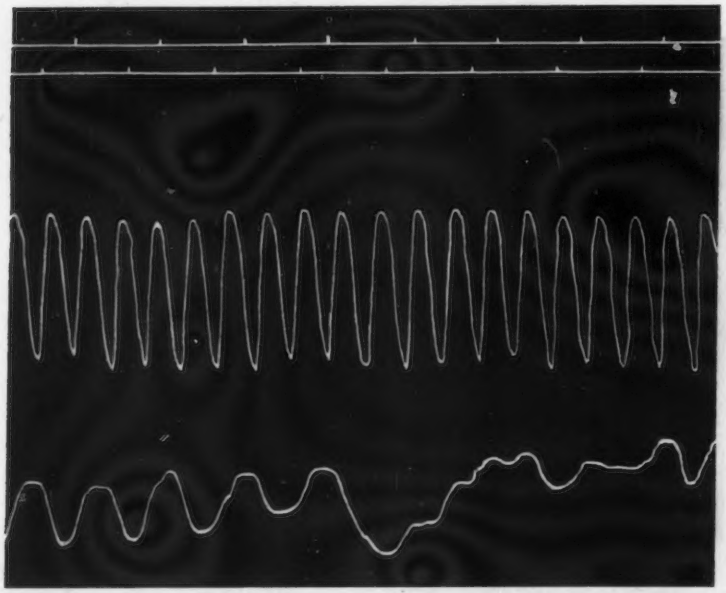

FIG. 16.—Tracings of rapid pronation-supination. The movements of the affected arm (below) were for a time regular though slower and of smaller amplitude than the normal, but grew irregular and the arm became more or less fixed in supination.

same or of other movements by the opposite limb, increases the irregularities indicates how dependent the rhythm of movement is on concentrated effort when cerebellar function is defective. One intelligent and observant patient remarked, "The movements of my left arm are done subconsciously, but I have to think out each movement of the right (affected) arm. I come to a dead stop in turning and have to think before I start again." It is significant that practice may improve the performance of the test.

A somewhat similar difficulty in executing alternating movements results from disease of the basal ganglia. To this fact we shall recur later.

Asynergy.—The term asynergy has been used so indiscriminately in the literature on the cerebellum that it is frequently difficult to decide the exact significance given to it. To some, as Tilney and Pike, Sager and Leiri, it means merely a disturbance in the normal co-operation of agonists and antagonists; others employ it in Babinski's original sense to signify a lack of co-ordination between wider groups of muscles, including those which should fix segments of a moving limb. In the latter sense the term is unnecessary as it would include symptoms of different origins. The question whether there is a specific disturbance in the normal relations of agonists and antagonists is more important. As Walshe (1927) has pointed out this relation is at the very foundation of the simplest reflexes and it is therefore improbable that it is in any way subject to cerebellar influence. Bremer concludes that no such disturbance has been proven, and Pollock and Davis have shown that it is not affected by removal of the cerebellum in animals. In his study on action currents Altenburger also found in man no alterations in the relations of agonists and antagonists during movement. My own observations indicate that no such disturbance exists in sufficient degree to play a part in the symptomatology of "cerebellar ataxia." Absence of the steadying influence which tonic antagonists normally exert on the prime movers in deliberate and accurate movements is, however, an important element, but this is merely a result of the general hypotonicity.

I have studied the relations of such simple synergies as extension of the wrist on flexion of the fingers, but though tracings show that when the fingers suddenly close wrist extension is less regular than normal, this does not appear to be an important or specific factor of "cerebellar ataxia."

Gait.—Owing to the wide distribution of these disturbances over the musculature of the trunk and limbs the irregularities of movement are greater the more complicated the latter is, and the larger the number of muscle groups employed in it. Abnormalities of gait, for instance, are often so prominent that an apparatus for the maintenance of equilibrium, or a special co-ordinating function for locomotion, have been assumed to exist in the cerebellum, but examination shows that they are a natural consequence of the same fundamental troubles which involve the whole motor system.

Nystagmus.—Although nystagmus is not common after ablation of the cerebellum in animals, and when observed has been attributed to injury of the vestibular nuclei or of other structures in the brain-stem, there is no

doubt that in man it is a common and direct result of cerebellar disease. Its essential feature is that the eyes fail to maintain postures and gradually swing towards their position of rest (slow phase), from which they are brought back by abrupt contractions of the oculogyric muscles (quick phase). This failure of posture is in every way comparable to that present in the rest of the motor system, but exceeds it in degree. The reason of this may be that the cerebellum has intimate anatomical and functional connections with the vestibular apparatus, and the latter has a dominant influence on ocular movements and postures.

Disturbances of associated and automatic movements.—A common symptom in even slight lesions of one side of the cerebellum is a failure of the ipsilateral arm to swing actively in walking synchronously with advance of the opposite leg; it hangs limply by the side or sways passively with movements of the shoulder. In progressive disease this is one of the earliest symptoms to appear, and it is usually the last to go on recovery. It cannot be readily explained by any of the primary motor disturbances with which we have already dealt, and may probably be regarded as a primary and fundamental symptom. It is also a feature of disease characterized by Parkinsonism due to destructive lesions of the corpus striatum; here it has been attributed to muscular rigidity, but as it may appear before onset of the rigidity this explanation is not adequate. The significance of such a special symptom in two conditions otherwise unlike will be discussed later.

FUNCTIONS OF THE CEREBELLUM AS REVEALED BY CLINICAL OBSERVATIONS.

From this analysis of the symptoms which result from lesions of the human cerebellum it is evident that the essential disturbances are: (1) postural hypotonia and impairment of certain reactions of the toneless muscles; (2) mild degrees of asthenia and fatigability of the muscles; (3) abnormalities in the rate, regularity and force of voluntary movements, and (4) failure of certain associated movements.

The disturbances included in each of these groups appear to be, as far as clinical examination can determine, primary or fundamental, that is not attributable to other factors. The hypotonia and defective postural adaptation are certainly elementary defects. It is possible that asthenia and fatigability are related to the hypotonic state of the muscles, but the disturbances in the rate and regularity of voluntary movement seem to be independent of it. This problem can be decided definitely only by investigation of the reactions of the hypotonic muscles by physiological methods. For the present they can be regarded as fundamental or elementary defects.

All the other symptoms included in "cerebellar ataxia," "inco-ordination" and "asynergy," are partly due to these elementary defects, in part the result of attempts of other portions of the nervous system to compensate the functions which are lost; the latter represent what Hughlings Jackson has called "forcing of other movements by overactivity of perfectly healthy nervous arrangements" (1888).

An analysis of the defect symptoms certainly affords no ground for assuming that the cerebellum contains a special centre for co-ordination, or that its function is the "co-ordination of motion" (Cobb). The inco-ordination which is undoubtedly associated with cerebellar disease is due

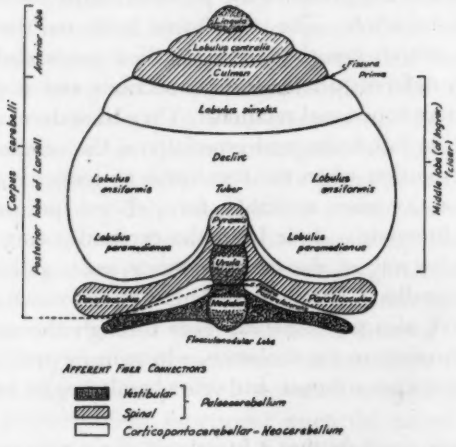

FIG. 17.—A diagram of the macaque cerebellum after Larsell (from Botterell and Fulton).

to more elementary disorders which impair the correct and harmonious execution of movements. In Hughlings Jackson's words, "It is only by entertaining vague notions about 'a co-ordination centre' (the lineal descendant of 'faculty of co-ordination') that we can speak of a destructive lesion of the cerebellum as causing inco-ordination of locomotion" (1888).

The problem then arises as to how the cerebellum normally assures postural tone, the grading and regulation of the rate and force of muscular contractions, and the execution of synkinesic automatic activities. In attempting to solve this problem it is necessary to recall its main connections with the rest of the nervous system.

Sherrington's term, "the head ganglion of the proprioceptive system,"

emphasizes the important influx to the cerebellum of afferent impulses which are largely concerned in posture. Through the spinocerebellar tracts and from the dorsal columns of the cord it receives messages from the deeper structures of the limbs and trunk, and from the vestibular apparatus, which plays such a large part in the postural reflexes, there is a constant stream of impressions. These spinal and vestibular impulses reach only the anterior and posterior segments of the cerebellum which represent the oldest parts of this organ (the palæocerebellum) (Larsell) (fig. 17). On the other hand by means of several paths through the correlation centres with which it is intimately connected this part of the cerebellum can send efferent impulses to the brain-stem and spinal cord.

But in man and the primates the palæocerebellum is a relatively insignificant part of the whole. The large lateral lobes and the middle portions of the vermis, which constitute the so-called neocerebellum, are newer structures with different anatomical connections and it may be assumed they have different functional relations. They have developed parallel with the growth of the fore-brain, and especially of the cerebral cortex, during that stage of evolution when the fore-limbs no longer required for stance and locomotion became available for delicate purposive movements (Brouwer and Biemond). It is from the cerebral cortex that their main afferents come by way of the cortico-pontine tracts and collaterals of the cortico-spinal bundles. Their chief efferent fibres, which arise in the neocerebellar nuclei, also pass cerebralwards through the superior peduncles and terminate mainly in the thalamus, which in its turn is intimately connected with the corpus striatum and other basal ganglia, as well as with the cortex.

It is, however, unlikely that a functional distinction comparable to this anatomical division exists between the so-called palæocerebellum and neocerebellum, and that the proprioceptive impulses from the spinal cord and vestibular apparatus, though they arrive in the former, have no influence on the latter. The uniform structure of the cerebellar cortex and the complex association fibres between different portions of it are strongly in favour of a uniformity, though not necessarily an identity, of function within it.

The neocerebellum of man, which owing to its size and position is most commonly involved by such local lesions as produce "cerebellar ataxia," has therefore predominantly cerebral relations, and it is probable that in the sense of these relations its functions must be sought (Walshe, 1927). Physiological experiments have provided evidence of this relationship; Russell and Rossi independently found that electrical stimulation of the surface of the neocerebellum alters the threshold of excitability of the

motor area of the opposite cerebral cortex, and Aring and Fulton observed "dramatic accentuation" of cerebellar signs when area 6a of the opposite frontal lobe was removed from animals in which these signs had decreased some time after extirpation of one side of the cerebellum. The predominance of symptoms of cerebellar defect in voluntary movement also indicates that it influences directly cerebral mechanisms which excite and integrate such movements rather than the reflex apparatus of the brain-stem and spinal cord; the latter, when isolated from the fore-brain, are in fact unaffected by ablation of the cerebellum.

It is a striking feature of acute cerebellar injury that its symptoms gradually decrease in intensity and may in time disappear. This fact has been universally recognized and has been explained by compensation by intact parts of the cerebellum and by other parts of the nervous system. But even in the acute stages of disease the disturbances may be to some extent reduced by training and by concentrated effort; for instance, a man who is unable to pronate or supinate his forearm, or flex and extend his fingers rapidly, may learn by repeated attempts to do so, and by practice may succeed in controlling to some extent the irregular movements of his ataxic limbs. As learning is predominantly a function of the higher levels of the nervous system, the cortex, and especially those parts of it concerned in the integration of voluntary movement, probably play a large part in compensation. There is further evidence of this in the facts that cerebellar ataxia becomes greater when attention is diverted from the active limb, and that the irregularities of movement increase after the administration of alcohol and narcotic drugs which depress attention (Holmes, 1918).

Hypotonia is certainly most prominent when the lateral lobes, which have cerebral connections, are injured, in fact according to several authors (Rademaker, Bremer, Sager) in lower animals rigidity of muscles follows removal of the palæocerebellum. This suggests that the neocerebellum may influence muscular tone by its action on the fore-brain.

Tone, it is true, depends on segmental reflexes, but Sherrington has shown that it may be modified by suprasegmental centres. As Bremer has pointed out, the cerebralward transfer of phasic motion necessitates a corresponding subordination of postural tone to the activity of the cortex of the fore-brain. By virtue of the proprioceptive impulses which it receives from all peripheral structures concerned in posture and in movement the cerebellum is in a position to send to the fore-brain an integrated influx which may serve in the control and distribution of muscular tone. As I wrote in my Croonian Lecture, the cerebellum in this way "helps to maintain and regulate the distribution of postural tone, and by its influence on the fore-

brain it aids in the regulation and the co-ordination of the modifications of tone in the necessary contractions and relaxations of muscles during movement" (1922).

The activities of the higher and less organized nervous centres are not dependent in the same degree as the lower on afferent impulses from any one source; when some are lost they may be replaced or compensated by impulses of other origin. This may be the explanation of the absence of obvious hypotonia in chronic and in stationary diseases of the cerebellum; its tonic functions are compensated by the activity of other centres, possibly by the cortex of the frontal lobe as Aring and Fulton have suggested.

Through the thalamus the cerebellum is also connected with the basal ganglia, including the substantia nigra, nucleus ruber and other subcortical centres, that is with those structures which belong to the so-called extra-pyramidal motor system. Though the functions of these masses of grey matter are still obscure there is general agreement that they are concerned in regulation of postural tone and in certain automatic activities and associated movements. Experimental physiology has as yet contributed little to our knowledge of the part they take in movement, but evidences of the important rôle they play in posture and in motor activity is presented from the clinical side by the disturbances of tone, irregularities of movement and spontaneous movements which characterize negative lesions of them. One of their functions seems to be to inhibit and control the tonic mechanisms of the brain-stem and spinal cord; when they are separated from the more caudal parts of the nervous system decerebrate rigidity results. The afferent impulses which regulate this activity may come from many sources, but it is probable that a cerebello-thalamic influx is one of the most important. During voluntary movement this cerebellar influx may be modified by the cerebral cortex through the cortico-pontine tracts; the size of the latter and their development parallel with the transference of volitional innervation to the cerebral cortex suggest they have an important influence in movements initiated in the cortex.

While the rigidity and exaggerated postural fixation of extrapyramidal disease can be regarded as "corresponding opposites" (Jackson) of cerebellar hypotonia, the diminution of certain automatic activities, as failure of the arms to swing in walking, the static tremor which may appear during maintenance of posture, the poverty of automatic movements, the slowness of motion and the difficulty in performing alternate movements, are symptoms common to disease of both the extra-pyramidal system and the cerebellum, and indicate a functional relationship between these two organs.

On this hypothesis there is superimposed on the postural and reflex mechanisms of the brain-stem a cerebello-striato-cortical apparatus concerned in the regulation of posture and of tone during voluntary movement. By virtue of the integration of the wealth of afferents it receives from all parts of the body and from the cerbral cortex the cerebellum is a controlling part of this mechanism.

Although Sherrington has shown that postural tone may fuse with and reinforce muscular contractions otherwise excited, clinical observations suggest that the *asthenia* of volitional movement in cerebellar disease is not due to lack of this tonic support. Rossi's discovery that stimulation of the surface of the cerebellum increases the excitability of the contralateral motor cortex is in favour of the view that the cerebellum exerts a reinforcing action directly on the cerebral centres through which voluntary motion is excited. Loss of postural tone supporting voluntary contractions may, however, contribute to the tendency to tire, but Bremer's view that *fatigability* as well as feebleness of movement is a fundamental symptom and due to an asthenia of the cortico-spinal motor apparatus deprived of cerebellar reinforcement, seems more probable.

The *abnormalities in the rate and regularity of voluntary movement* cannot be explained by disturbances of the executive motor mechanisms of the brain-stem and spinal cord as when these are isolated from the forebrain removal of the cerebellum does not affect their activities. Nor can they be attributed to the toneless state of the antagonists as they appear in movements against resistance in which the opposing muscles are not actively concerned. We must therefore conclude that they are due to disorder in the cerebral mechanisms of voluntary movement, as a result of which there is a delay in initiating cortico-spinal innervation, a lack of uniformity in the intensity of corticofugal discharges and a failure to arrest or inhibit these discharges with normal promptitude.

The conclusions can be drawn that, in addition to regulating postural tone, the cerebellum reinforces or tunes up the cerebral motor apparatus, including subcortical structures with motor functions, so that they respond promptly to volitional stimuli and the impulses from them which excite muscular contractions are properly graded.

In his classical contributions to the physiology of the cerebellum Luciani described as the three symptoms of cerebellar defect: atonia, astasia and asthenia. These three symptoms occur in man as a result of acute cerebellar lesions and by them the irregularities of movement which constitute cerebellar ataxia can be fully explained.

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SOME OBSERVATIONS ON THE NATURE OF VIBRATORY SENSIBILITY.[1]

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THE nature of vibratory sensibility has long been a matter of conjecture and controversy, as revealed by the voluminous literature concerning it. The question as to whether or not it constitutes a distinct modality of sensation cannot be said to be definitely settled, it being variously stated that it is an integral part of touch, of pressure, or an entity in itself.

The central representation of vibratory sensibility seems more definitely established and must certainly be localized in the sensory cortex. It has also been shown that the pathway traverses the thalamus, while in the spinal cord it is generally conceded (Gordon, 1936) to be in the homolateral posterior columns, as shown by the loss of vibratory acuity on the homolateral side after hemisection of the cord. However, the peripheral distribution, and the type and location of the end-organs involved are far from clear, and it is with these questions that this paper concerns itself.

METHOD.

Because of the greater ease of control and measurement of the vibratory stimulus with an electromagnetic vibrator than with a tuning fork, no matter how ingeniously contrived, the former type of instrument was chosen for this work. The actual instrument used presented no departures in principle from those devised by other workers (v. Bogh (1935), Sitzepfand (1935) and Hugony (1935)). It consisted of an electro-magnet, the pole-piece of which is caused to vibrate by the passage of alternating current through the coil. This is derived from a beat-frequency oscillator capable of generating current at frequencies from 30 to 15,000 cycles per second, of essentially sine-wave form. The voltage across the coil of the electromagnet and the current through it are controlled by means of a potentio-

[1] Work done while Dr. Newman held a Rockefeller Fellowship, Dr. Doupe a Halley-Stewart Research Fellowship, and Dr. Wilkins a Fellowship of the American College of Physicians.

meter, and measured by suitable meters. Thus both the frequency and amplitude of the stimulus are variable at will, and accurately mensurable. Since it has been shown that for a given frequency the amplitude of vibration is fairly closely proportional to the current passing through the coil, this figure in milliamperes has been used to designate the intensity of the stimulus. The pole-piece, which actually delivers the stimulus, is a square piece of metal measuring 9 by 9 mm., and is ordinarily applied to the area to be tested by holding the handle of the instrument, about 17 cm. long, at the end and allowing it to press on the skin by its own weight, thus maintaining a fairly constant pressure of about 450 grams per square centimetre. At other times, the pole-piece is just maintained in contact with the skin, without perceptibly deforming it. The first type of contact will be termed heavy, the second light. In all cases the vibratory movement is roughly perpendicular to the skin surface.

It was found by this technique that the threshold for vibratory sensibility, as measured by the intensity of stimulation at which the subject first became aware of vibration of the instrument when the current was gradually increased, remained quite constant for the same locality in the same individual from time to time, especially with heavy pressure. With light pressure the results were less constant, owing to difficulty in maintaining a constant pressure of contact. Such was the constancy of thresholds obtained, however, that there could be little doubt of changes which appeared after any experimental intervention being connected with that procedure, and not being due to chance fluctuations.

All the experiments were carried out with a frequency of 200 cycles per second as the standard stimulus. This was found to be the optimal frequency, as has been noted by other observers (v. Bogh (1935) and Sitzepfand (1935)). Both lower and higher frequencies gave higher thresholds, and with the intensities at our disposal 500 to 600 cycles was the highest that could be perceived except in the hands, and particularly in the fingers, where up to about 1,000 cycles could be discerned. In all cases where there was a change in threshold brought about by anæsthesia, all frequencies seemed to be affected to about the same degree, with no tendency for either the higher or the lower to drop out first.

Procedures and Results.

For the evaluation of the results to be reported it was necessary to know the comparative thresholds for light and heavy contact in the regions used in these experiments. Table I, which gives the averages of several experiments in normal young adults, shows that for heavy contact the finger-tip

was the most sensitive, then the forearm and calf, and lastly the forehead. The threshold for light contact varied in the same way, and was close to that for heavy contact in the case of the finger and forehead, but above it in the case of the forearm and calf. Little difference was found whether the contact overlay bone or muscle.

TABLE I.—AVERAGE THRESHOLD AT DIFFERENT SITES.

	Heavy contact	Light contact
Finger tip ...	0·07 milliamp.	0·10 milliamp.
Forearm ...	0·4 ,,	3·0 ,,
Calf	1·0 ,,	5·0 ,,
Forehead ...	3·5 ,,	5·0 ,,

It was also necessary to know to what degree the tissues could conduct vibrations from an insensitive to a sensitive area. To determine this, a sphygmomanometer cuff was placed around the forearm and inflated to a pressure of 200 mm. Hg for fifty minutes, which caused complete anæsthesia below the cuff. The threshold for heavy contact on the radial styloid process rose from 0·06 to 0·4, while for light contact it rose from 0·3 to 5·5, and the sensation was now referred to the region of the elbow. The capacity of the bones to act as vibrators was further shown in two cases with section of the left second, third, fourth and fifth thoracic posterior roots. In the denervated area the threshold for heavy contact was only slightly raised, and was not affected over the denervated half of the sternum.

DEEP STRUCTURES.

That vibration sense may be mediated by sensory endings in deep structures was shown in the following way. In three individuals on thirteen occasions the threshold for heavy contact was determined several times on four spots on the forearm or calf. Into one spot 3 c.c. of 2 per cent. novocain with adrenalin were injected subcutaneously so that an area of skin 3 cm. in diameter was rendered anæsthetic. The vibratory threshold was then measured repeatedly on all the spots and no rise in threshold was found on the anæsthetic one. In a few instances the threshold was lowered locally by the novocain. In five further experiments a cutaneous nerve in the forearm, calf, or thigh was anæsthetized with novocain. This did not cause any change in threshold with heavy contact in the distribution of the nerve anæsthetized, although there was complete anæsthesia of the skin.

Seven experiments were then done in an endeavour to modify the appreciation of vibration by anæsthetizing deep structures while leaving superficial sensation intact. This was done by the use of localized pressure

applied by means of a clamp with one bearing surface large and the other small—the latter being placed over the nerve—or by the injection of 2 per cent. novocain and 1:60,000 adrenalin into the trunks of the ulnar and median nerves at the elbow, and the superficial peroneal nerve at the neck of the fibula. Block of the ulnar nerve at the elbow caused, among other things, paralysis of the flexor carpi ulnaris and of the medial half of the flexor profundus digitorum, and anæsthesia to all forms of sensation in the little finger. Block of the radial nerve on the anterior surface of the lateral condyle of the humerus produced paralysis of the extensor muscles of the wrist which lie on the posterior aspect of the forearm. Block of the superficial peroneal nerve caused paralysis of the peroneal group of muscles. Cutaneous sensation over these groups of paralysed muscles, however, remained intact. In these experiments two or three points over the paralysed muscles were selected, with a similar number of points over adjoining muscles to serve as controls. In the case of the ulnar nerve experiments the 2nd, 4th and 5th digits were examined. After two or three readings at each site had been taken and a reasonably steady base-line established, the blocking procedure was begun. Thereafter readings were taken at each site every ten minutes for forty to fifty minutes, at which time a maximal effect seemed to have been produced. The last two readings were then compared with the findings before the induction of the block, and the percentage rise in threshold calculated. The average rise at the sites over the paralysed muscles was 70 per cent., while the average rise at the control sites was 10 per cent. Table II sets forth the results of each experiment.

To control the possibility that the flaccidity of the paralysed muscles might have been responsible for the rise in vibratory threshold another experiment was done. Observations were made on the posterior aspect of the forearm with the underlying muscles voluntarily contracted and relaxed. No significant difference in threshold was found with the muscle in these two states.

In order to determine whether direct stimulation of the periosteum is responsible for the sensation of vibration, a large area on the anterior surface of the tibia was infiltrated with 2 per cent. novocain and adrenalin. This procedure abolished all superficial and deep sensibility in the area injected. No rise in vibratory threshold to heavy contact was found when compared with the pre-injection acuity, and to control readings on the other leg. Thus it was evident that direct stimulation of the periosteum by the stimulating instrument was not an important factor in the appreciation of vibration.

In the experiments in which the ulnar nerve was blocked, it was found that vibration sense was completely abolished in the 5th digit. This was particularly true if slight traction were exerted on the distal phalanx to prevent the conduction of vibration from bone to bone. In the 2nd and 4th digits the threshold for heavy contact was unaffected. However, on the medial side of the 4th digit, where there was loss of light touch, the

TABLE II.—VIBRATORY THRESHOLD.

Exp. No.	Procedure	Over paralysed muscle			Control		
		Average before*	Average after*	% change	Average before*	Average after*	% change
321	Novocain anæsth. ulnar N.	0·6	1·2	+100	1·0	1·4	+40
		0·5	0·7	+ 40	0·5	0·6	+20
322	Novocain anæsth. ulnar N.	1·6	2·4	+ 50	3·9	3·5	−10
					4·0	2·4	−40
					1·9	2·5	+30
					1·2	1·9	+58
324	Pressure anæsth. ulnar N.	2·0	2·1	+ 5	3·1	4·0	+29
		2·4	2·0	− 16	3·1	2·7	−13
		2·6	6·0	+130			
327	Pressure anæsth. ulnar N.	0·7	2·2	+214	1·0	1·1	+10
		0·8	1·5	+ 88	0·67	0·72	+ 7
328	Pressure anæsth. radial N.	0·15	0·32	+133	0·19	0·17	−10
		0·23	0·25	+ 8			
		0·14	0·33	+136			
326	Pressure anæsth. sup. peroneal N.	0·7	0·8	+ 14	2·0	0·75	−65
		2·8	4·6	+ 64	2·9	2·8	− 3
	on release	0·8	0·8	0			
325	Pressure anæsth, sup. peroneal N.	3·0	5·2	+ 73	4·2	5·1	+21

* Figures express in milliamps the intensity of the vibratory sensibility.

threshold for light contact was raised. It was apparent from this that the preservation of the acuity of perception of vibration with heavy contact in the 2nd and 4th digits was not due to receptors lying in the skin. It was also observed that the rise in vibratory threshold in the 5th digit was, along with a diminution in postural sense, the first demonstrable effect of pressure on the ulnar nerve, and the threshold of vibratory sense had greatly risen before any paresis of the muscles was evident. The intact threshold to heavy contact on the medial side of the 4th digit and the results of a further experiment reported below showed that this loss in vibratory sense to heavy contact was not due to interference with cutaneous sensibility. The facts that the threshold had risen before any muscular weakness was evident, that vibration sense was completely abolished while many of the muscles supplying long tendons to a 5th digit had an intact innervation.

and that no rise in threshold occurred in the 2nd and 4th digits whose small muscles were also paralysed, indicated that the sensation of vibration was partly mediated in the finger by structures lying deeply within the finger itself and unassociated with muscles and tendons.

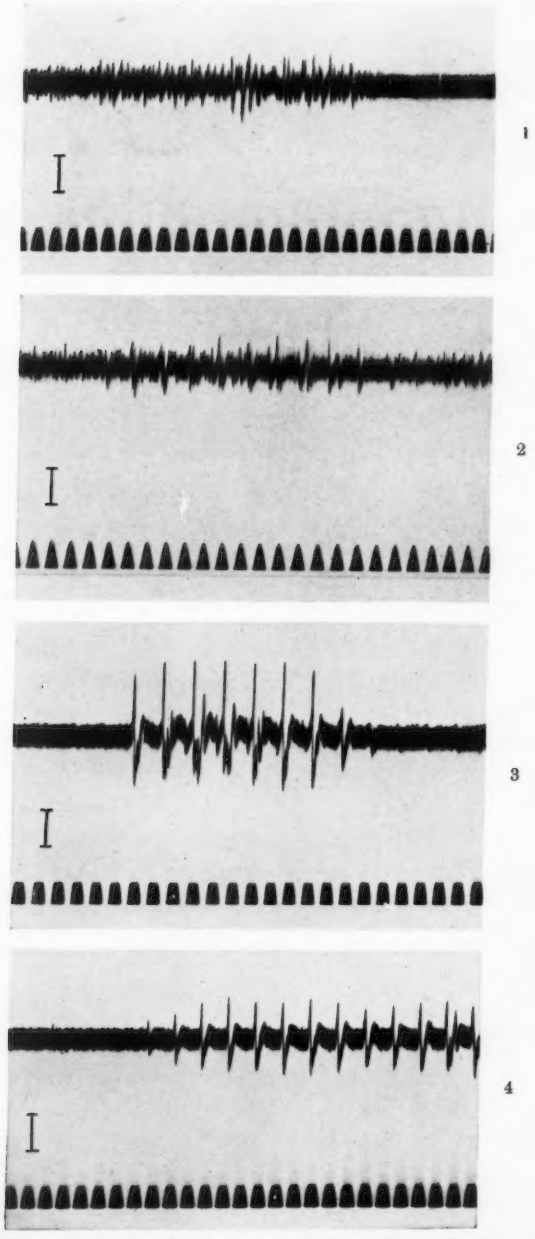
Superficial Structures.

When the vibrating surface was applied so that it was just in contact with the skin the threshold was as a rule much higher than that with heavy contact. This was particularly true in the limbs at those sites where there was much subcutaneous tissue. It has already been stated that on the finger-tips and forehead there was little difference in threshold between the two types of contact. The question therefore arose as to whether the sensation of vibration could be mediated by way of receptors in the skin, or depended entirely on the transmission of the vibrations to deeper structures. The following observations bear on this question.

To determine if receptors were located in the skin which could respond at frequencies usually employed in testing vibration sense, Dr. G. L. Brown kindly performed the following experiment. A purely cutaneous branch of the saphenous nerve of a cat was dissected out, and placed across two electrodes. Action potentials from this nerve were suitably amplified and recorded on moving bromide paper, a Matthews oscillograph being used. Light stroking of the area of skin innervated by this nerve produced discharges as shown in fig. 1. The insulated base of a tuning fork with a frequency of 64 cycles per second was then lightly applied to the area, with production of large action potentials at the same frequency as the vibrations of the fork, as seen in fig. 2. Even larger potentials were produced when an arm rather than the base of the fork was used to stimulate the skin (fig. 3). Similar potentials at the same frequency as the vibrations of a fork of 450 cycles were also obtained. The same potentials were obtained when the bit of skin was dissected free from the leg (fig. 4). Crushing the nerve abolished the potentials; furthermore, they did not appear when a piece of moist thread was substituted for the nerve. It seemed probable, therefore, that the quality of vibration might be recognized by receptors lying in the skin, which initiate rhythmical action potentials when subjected to the stimulus of the tuning fork.

In one subject the 3rd digit was rendered anæsthetic by iontophoresis with 2 per cent. cocaine, causing a sensory loss to pin-prick and light touch, without disturbance of proprioceptive acuity. The threshold to vibration with heavy contact remained unchanged, and similar to that in the second

PLATE I.



Action potentials from a cutaneous nerve of the cat. Calibration shows deflection caused by 20 microvolts. Direction of negative deflection is upwards. Time in 1/100 seconds.

FIG. 1.—Response to stroking skin.
FIG. 2.—Response to stimulation by base of 64 cycle tuning fork.
FIG. 3.—Response to stimulation by arm of 64 cycle tuning fork.
FIG. 4.—Response to stimulation of isolated skin by arm of 64 cycle tuning fork.

To illustrate article by H. W. Newman, J. Doupe and R. W. Wilkins.

finger. The threshold for light contact was raised, but progressively returned to the original level as cutaneous sensation returned. However, anæsthetization of the skin of the forearm by the local injection of 2 per cent. novocain and adrenalin was found to cause only irregularly a rise in threshold to light contact. That this might be attributed to the great sensitivity of the deep receptors in this region was shown by an experiment in which the ulnar nerve was anæsthetized by pressure at the elbow. On sites overlying the paralysed muscles in the forearm, but on unaffected skin, the threshold to both heavy and light contact rose slightly, presumably due to anæsthesia of the deep receptors. Then, during the period of the pressure block, 2 per cent. novocain was injected subcutaneously into one of the sites over a paralysed muscle. This resulted in a further marked rise in the threshold to light contact. It was thus seen that only when the deep receptors, with their great sensitivity, are anæsthetized does the cutaneous appreciation of vibration become evident.

In the upper arm a slightly different relationship between the sensitivity of the deep and superficial receptors seems to exist. Thus in a subject who had had a section of the left 5th cervical dorsal root there was a very marked rise in the threshold to light contact over an oval area 10 by 5 cm. on the lateral aspect of the upper arm co-extensive with the area for diminished touch. However, no rise in threshold for heavy pressure was demonstrable, even over the partially paralysed and wasted deltoid.

On the forehead and tongue results differing from those on the forearm were obtained. In these situations the threshold for light and heavy contact was about equal, and was similar to that for light contact on the forearm. Anæsthetization of the skin of the forehead by the injection of novocain, or of the mucous membrane of the tongue by the topical application of cocaine, raised the threshold to both types of stimulation. In these regions, therefore, the deep receptors, if they be present, have a comparatively high threshold. Observations on a subject who had had a section of the sensory root of the left 5th cranial nerve confirmed this deduction. It was found that an exceedingly high threshold to both light and heavy contact existed on the left side of the head and tongue. This high threshold persisted unchanged to within 3 mm. of the midline, despite the fact that vibration was mechanically transmitted and could easily be detected by the observer at points all over the skull. Thus in this situation mechanical transmission by bone seems not to be a factor. This is in contrast to the experiment reported on the forearm, where stimulation at the anæsthetized wrist could be felt at the elbow.

Afferent Pathways.

The peripheral fibres conducting the sensation of vibration from light and heavy contact appeared to be of the same size, and similar to those mediating touch and passive movement. This was shown by the observation that the sensitivity to vibration, touch, and passive movement was very easily affected by pressure on the nerve, but disappeared comparatively late when novocain was the anæsthetizing agent. However, an essential difference between the appreciation of vibration according to whether light or heavy contact were employed was demonstrated in subjects with lesions of the spinal cord. In two cases of unilateral section of the spino-thalamic tract no difference in threshold to either type of stimulus between the normal and anæsthetic sides was evident. However, the sensation produced by light contact was subjectively different, being less "sharp" on the analgesic side, and corresponded to the change in appreciation of light touch. The sensation with heavy contact was not altered. In a subject with disseminated sclerosis who had a typical Brown-Séquard syndrome, vibration sense to heavy contact was lost in the lower limb where appreciation of passive movement was defective. However, at both great toes vibration sense to light contact was normal, as was the appreciation of light touch.

Discussion.

In presenting the above results several deductions have already been made. It has been pointed out that the sensation of vibration can be mediated by receptors lying both in the skin and in the deeper tissues. The relative acuity of these two sets of receptors has been found to vary in different parts of the body.

A consistent rise in threshold to vibratory stimulation over muscles, the nerve supply of which had been functionally interrupted, indicates that there are receptors for this sensation in muscle itself. Periosteum is probably not an important factor, as shown by the experiment in which it was anæsthetized over the tibia without any loss of vibratory acuity. The importance of bones in mechanically transmitting the vibrations to the sensitive structures has been demonstrated in the experiment where the wrist was rendered anæsthetic. The experiment with ulnar nerve block indicates that tendons are probably not an important factor, for the tendon innervation to the little finger was largely intact, yet vibration was not perceived when mechanical transmission by the bones was interrupted. It has also been shown that some of the deep receptors are not associated with muscles.

The vibratory sensation from the deep receptors in the 5th digit has been shown to be affected similarly as the sensation of passive movement when the ulnar nerve was anæsthetized. Stopford (1930) has shown, and we have confirmed his observations, that passive movements are recognized at the joints of a digit the muscles and tendons to which have been deprived of their nervous connections. The recognition of vibration in such digits was similarly unaffected. Ecklin and Fessard (1937) have recorded from nerves to muscles, in the cat, action potentials of a frequency synchronous with the vibrations of a tuning fork applied to the muscles or their tendons. It was their opinion that stretch receptors, which are proprioceptive in nature and at least partially responsible for the perception of passive movement, were the source of the electrical activity demonstrated. The present results also indicate that the sensation of vibration is in part dependent on receptors in muscle. The peripheral nerve fibres conveying the sensations of vibration and passive movement are similarly susceptible to compression and novocain. Lesions of the posterior columns abolish the perception of both passive movement and vibration from deep structures, while lesions of the spinothalamic tract do not affect it.

Thus all the evidence seems to indicate that there is a very close relationship between the senses of vibration and of passive movement. So similar, indeed, are the sites of their peripheral receptors, the characteristics of the nerve fibres, and the central pathways, that it seems probable that they are mere variants of a single mode of sensibility. However, it must be remembered that purely cutaneous stimulation has also been shown to be appreciated as vibration. The experiments carried out by Brown and recorded above show that certain potentials of a similar character to those produced by Ecklin and Fessard could be obtained from a nerve to an isolated piece of skin. It is probable that this cutaneous appreciation of vibration bears the same relationship to touch as the appreciation by the deeper tissues does to passive movement. Vibration cannot, therefore, be said to be a specific modality. The sensation is the result of rapid repetitive stimulation of touch or proprioceptive endings.

Conclusion.

It has been shown that the sensation of vibration may proceed from stimulation of receptors in the skin and in the deeper structures. It is probable that the receptors in the skin are the same as those concerned with the sensation of touch, while those in the deeper tissues are closely related to, if not identical with, the receptors mediating the sense of passive movement.

The animal experiments recorded here were performed by Dr. G. L. Brown at the National Institute for Medical Research, Hampstead, to whom the authors wish to express their thanks.

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THE SYSTEMIZATION AND CENTRAL CONNECTIONS OF THE SPINAL TRACT AND NUCLEUS OF THE TRIGEMINAL NERVE.

A CLINICAL AND PATHOLOGICAL STUDY

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Introduction.

The nuclei of the trigeminal nerve extend from the most cephalad level of the midbrain to the second cervical segment of the spinal cord and are at every level linked to secondary afferent and efferent neurones. It is therefore apparent how greatly they are exposed to morbid processes and how diverse are the symptoms that may result.

Despite the thoroughness with which the anatomy of the principal fibre tracts was worked out during the closing years of the last century certain obscurities still remain, particularly in regard to the extent and quality of the representation within the spinal tract and its nucleus and to the exact position of the central trigeminal pathway. With certain exceptions presently to be specified these problems have not evoked much inquiry of recent years, and the time seems opportune for their re-examination. Before proceeding to an analysis of the clinical and pathological material which forms the basis of these investigations it will be advisable to give a review of past and current opinions and to attempt a critical assessment of the clinical, pathological and experimental evidence on which they were founded.

Historical Review.

The probable segmental representation of the spinal tract and nucleus of the trigeminal nerve.—Bregmann (1892) carried out differential section of the sensory root in rabbits and studied the resulting degeneration by the Marchi technique, and arrived at the following conclusions:—

Within the spinal tract the fibres from the mandibular nerve occupy the most dorsal and those from the ophthalmic nerve the most ventral part of the tract. The fibres from the maxillary nerve lie in an intermediate position. Further, the sets of fibres from the three divisions end at separate levels. The fibres from the ophthalmic nerve end at about the second cervical segment in the most caudal part of the spinal tract. The fibres from the maxillary nerve terminate rather more cephalad but a few descend as low as the first cervical segment. The fibres from the mandibular nerve end in the upper part of the medulla oblongata. From this summary it will be seen that the three divisions of the trigeminal nerve end at levels which are in the inverse order to the peripheral distribution. Wallenberg (1896), in an experimental study on the position of the central trigeminal tracts, produced lesions at various levels of the spinal tract in rabbits and his conclusions were in agreement with those of Bregmann.

Bochenek (1901) avulsed the peripheral divisions of the trigeminal nerve in two rabbits and, at the end of sixty days, examined the brain stem by the Marchi technique. He confirmed Bregmann's findings in regard to the relative position taken up by the three divisions within the spinal tract, but he found no evidence that the fibres from the three divisions ended at distinct levels and, after avulsion of the mandibular nerve, he traced degenerated fibres to the level of the first cervical segment. His results cannot escape criticism. In the first place it is unwarranted to assume that avulsion of one peripheral division will lead to no more than selective injury to the ganglion cells of that division, it may possibly have led to more widespread damage within the trigeminal ganglion and there is no evidence that Bochenek examined this. In the second place Bochenek did not examine the brain stems serially and he made no examination of the second cervical segment of the spinal cord.

Spiller and Frazier (1901) carried out experiments bearing on this problem in order to show that the operation of sensory root section was more satisfactory than excision of the trigeminal ganglion for the cure of trigeminal neuralgia, and to this end it was necessary to show that regeneration did not occur after division of the sensory root. They divided the sensory root in dogs, and Spiller traced the resulting degeneration in the spinal tract. In some of the dogs Frazier had been able to spare the

ophthalmic fibres and, on the basis of the resulting partial degeneration in the spinal tract, Spiller affirmed that the fibres from the three divisions occupied definite areas in the spinal tract, exactly as Bregmann and Bochenek had shown in the rabbit. Their results threw no light on the problem of the levels at which the fibres from the three divisions terminate.

Van Valkenburg (1911) found that in all types of vertebrate the ventrally placed fibres in the spinal tract mediated impulses from the integument of the anterior end of the head and that this ventral contingent of fibres extended furthest caudalward. The dorsally placed fibres were related to the mandibular region. They terminated cephalad of the ventral fibres and their point of termination was, to a great extent, determined by the terminal regions of viscerosensory and visceromotor nerves. Van Valkenburg's views were later supported by Frazier (1929), who stressed the essential independence of the ophthalmic nerve despite its fusion with the other peripheral divisions in the trigeminal ganglion. Further support was given by Kappers (1936) who stated that in most vertebrates the fibres from the ophthalmic nerve lie most ventral in the spinal tract and extend furthest in a caudal direction, even reaching the spinal cord. The maxillo-mandibular fibres, on the other hand, terminate in the medulla oblongata. Thus, he stated, stimulation on the top of the head leads to motor responses from the trunk and limbs while stimuli from the mouth region find expression in movements of the face and jaws through the innervation of cranial nerves.

The clinical approach to the problem began with the publication by Wallenberg (1895) of a case of occlusion of the posterior inferior cerebellar artery. The sensory loss in the trigeminal area in this case led him to adopt the view that in man the representation of the peripheral divisions within the spinal tract was similar to that described by Bregmann in the rabbit.

A different view of the segmental representation within the spinal tract was put forward by von Sölder (1899) and Schlesinger (1899, 1902) from a consideration of the distribution of sensory loss in syringobulbia. Schlesinger's views were founded on an examination of fifty-six cases of which eighteen came to post-mortem examination. In a purely clinical study von Sölder had stated that extension of the syringomyelic process from the second cervical segment to the spinal tract and nucleus of the trigeminal nerve caused sensory loss to appear first on the scalp. As the lesion extended cephalad the anterior border of the area of sensory loss advanced towards the nose and mouth. Schlesinger confirmed this observa-

tion. He postulated that the fibres from the fronto-cranial territory of the ophthalmic nerve terminated in the most caudal part of the spinal tract. The fibres of the mandibular nerve terminated at a slightly higher level and those from the maxillary nerve higher still. Finally the fibres from the nasal portion of the ophthalmic nerve terminated highest of all. From the clinical findings in syringobulbia and vascular lesions of the brain stem Kutner and Kramer (1907) arrived at similar conclusions. It is worthy of note that in those cases in which the lesion was vascular in origin the distribution of the sensory loss did not conform to von Sölder's and Schlesinger's hypothesis.

Spiller (1908) reported two cases of occlusion of the posterior inferior cerebellar artery in one of which post-mortem examination was obtained. He considered that the representation within the spinal tract was in terms of the peripheral divisions and that a lesion of the lowest part of the spinal tract and nucleus would lead to analgesia in the territory of the ophthalmic nerve. If the lesion involved the lower two-thirds of the spinal tract and nucleus then analgesia in the territory of the maxillary nerve would be superadded.

Dejerine (1914) stated that the representation in the spinal tract from below upwards was in terms of concentric zones which converged on the bucconasal orifices. It will be seen, however, that this is merely a slight variation of von Sölder's and Schlesinger's views and the diagram which he gave in illustration is identical with that figured in Schlesinger's monograph. It is quite clear (and Dejerine fully admitted it) that this hypothesis of concentric zones was based exclusively on the findings in syringobulbia. This same hypothesis was put forward by Woods (1913) in explanation of the distribution of the sensory loss which he had encountered in two cases of syringobulbia. Autopsy was obtained in only one of these and there were bilateral cavities in the medulla oblongata in the usual situation (in the formatio reticularis and in the plane of the intramedullary fibres of the glossopharyngeal and vagal nerves and extending cephalad almost to the pons). The spinal tracts and nuclei were stated to have been unaffected either by cavitation or gliosis. The analgesia on the face, which spared the upper lip and perinasal region, was attributed to an interruption of the secondary sensory neurone. The brain stem was not examined in serial section apparently but neither cavity was continuous in its vertical extent, and bridges of normal tissue intervened at several places. Stopford (1924), from the study of the blood supply of the pons and medulla oblongata and of cases of occlusion of the posterior inferior cerebellar artery, stated that "there is strong anatomical and

clinical evidence in support of the view that the most cephalic part of the spinal nucleus of the trigeminal receives fibres from the anterior maxillary division and it appears highly probable that the intermediate part is connected with the superior maxillary division; whilst the ophthalmic division terminates in the caudal part." The two anatomically verified cases of syringobulbia reported by Taylor, Greenfield and Martin (1922) may be cited as evidence that the sensory loss in this disease by no means always invades the face in the manner regarded as typical by Schlesinger and Dejerine. In both these cases the analgesia and thermanæsthesia invaded the trigeminal area from above downwards and, from the beginning, the area of sensory loss extended to the midline of the face. Jonesco-Sisesti (1932), basing his conclusions on eleven cases of syringobulbia with four post-mortem examinations, stated that the territory of the ophthalmic nerve is the most frequently and earliest affected. Next in order of frequency the maxillary and mandibular nerves become affected. He attributed the early appearance of sensory loss in the territory of the ophthalmic nerve to the destruction by cavitation of the most ventral fibres of the spinal tract. A critical examination shows that this is not a satisfactory explanation of the type of sensory loss present in his cases. While in many instances the most ventral fibres in the spinal tract were most severely affected, in an equal number of cases the lateral extremity of the cavity fell short of the periphery and in such instances the most ventrally placed fibres actually appeared least affected. Furthermore this hypothesis takes no account of the possible effect of the cavity on the second sensory neurone although the characteristic dorsally placed cavity, lying obliquely between the 4th ventricle and the point of emergence of the glossopharyngeal and vagal nerves, must bar the passage of the second sensory neurone. Finally this hypothesis fails to take into account the possible effects of the gliosis which always surrounds the actual cavity.

Recently Sjöqvist (1937) has made clinical observations following section of the spinal tract in man. In four patients suffering from trigeminal neuralgia he made a horizontal incision into the spinal tract in a plane situated midway between the calamus and the junction of the medulla oblongata with the pons. The incision was placed just caudal to the most caudal rootlet of the vagus and extended into the medulla oblongata to a depth of 3·5 mm. Subsequently the patients showed analgesia and thermanæsthesia accurately limited to the territories of the ophthalmic and maxillary nerves. In some there was a light hypoalgesia in the territory of the mandibular nerve. These results do not give absolute

proof that that part of the spinal nucleus related to the mandibular nerve lies at or just cephalad to the plane of the section, for it is possible that the most dorsal fibres in the spinal tract were preserved. Only a dorsal prolongation of the section, to include a part at least of the inferior cerebellar peduncle, would ensure that the whole of the spinal tract was cut. Nevertheless Sjöqvist's observations afford the strongest possible evidence in favour of the view that the segmental representation in the spinal tract is in terms of the peripheral divisions and that the order is inverted. They are incompatible with the view that the representation is in terms of concentric zones or circles which converge on the nose and mouth. The problem concerning the level at which the mandibular fibres terminate now seems to have been decided, for, in a more recent investigation, Sjöqvist (1938) has succeeded in obtaining analgesia of the whole trigeminal area by means of an incision into the spinal tract at the mid-olivary level.

An examination of general neuroanatomical and neurological writings discloses, as might be expected, a striking lack of uniformity in regard to the account of the probable segmental representation in the spinal tract. Winkler (1921), in an account of the structure of the spinal tract and nucleus, agreed with Bregmann's conclusions and considered that they applied in man. He maintains that the substantia gelatinosa proper does not extend higher than the most cephalad rootlets of the glossopharyngeus. Between this plane and the main sensory nucleus he recognizes a distinct nuclear mass ("nucleus b") morphologically identical with a part of the main sensory nucleus. This differentiation of the spinal nucleus adds to the complexities of the problems which the spinal tract and nucleus present. As yet there does not appear to have been any attempt to correlate this anatomical differentiation with normal and pathological function.

It is interesting to observe that those authors who have approached the problems of the spinal tract from the clinical standpoint accept the view first advanced by von Sölder and Schlesinger, and have based their views on the segmental representation in the spinal tract on the findings in syringobulbia, but no case of syringobulbia without complete histological examination should be admitted as positive evidence in favour of either hypothesis.

Those anatomists who have studied vascular lesions of the brain stem have never subscribed to the hypothesis of representation in terms of concentric zones and a search of the literature has failed to disclose any instance of vascular disease in which the sensory loss on the face lent support to this hypothesis.

The qualities of sensation mediated by the spinal tract of the trigeminal

nerve.—Hun (1897) reported a typical example of occlusion of the posterior inferior cerebellar artery. There was analgesia and thermanæsthesia on the left side of the face with a crossed analgesia and thermanæsthesia on the trunk and limbs. Tactile sensibility was everywhere normal. The patient survived for three years and during this time the sensory disturbances on the face remained unaltered. Post-mortem examination showed the characteristic softening in the retro-olivary region. From these observations Hun postulated that the fibres of the sensory root of the trigeminal nerve on entering the pons are grouped in functional divisions and that impulses underlying pain and temperature pass in the spinal tract whilst touch is mediated by fibres passing to the main sensory nucleus. Subsequent reports of examples of occlusion of the posterior inferior cerebellar artery have almost always supported this view. Spiller (1915), in a presumed case of disseminated sclerosis, found gross tactile anæsthesia over the entire left side of the face with analgesia and thermanæsthesia on the entire right half of the body. He localized the lesion in the left main sensory trigeminal nucleus and with sparing of the left spinal tract (there was a very light thermanæsthesia over the territory of the left ophthalmic nerve). The interest in this case lies in the fact that pain and thermal sensibility were preserved together with complete tactile anæsthesia, thus providing strong evidence that the main sensory nucleus is the sole synaptic junction for tactile impulses. On the other hand anatomical studies have given presumptive evidence that touch is mediated by both the main sensory and spinal nuclei. Cajal (1909), Gerard (1923) and Windle (1926) have shown that, in the fœtal mouse and pig, the majority of the fibres of the trigeminal nerve on entering the pons divide into ascending and descending branches. The ascending branches end almost at once in the main sensory nucleus and the descending branches pass downwards to constitute the spinal tract. It is plain that a nervous impulse traversing such a bifurcating fibre must pass equally to the main sensory nucleus and to the nucleus of the spinal tract and since it seems certain that pain has no representation in the main sensory nucleus these observations are difficult to interpret. Gerard suggested that pain is mediated by the fine non-medullated fibres which pass without bifurcation into the spinal tract. However, Windle's studies showed that many of the fine non-medullated fibres do bifurcate. The purely anatomical evidence is thus rather equivocal.

From the cases of Sjöqvist it can be affirmed that a lesion of the spinal tract causing analgesia and thermanæsthesia is compatible with normal tactile sensibility. Occasionally some degree of tactile hypoæsthesia (but

never anæsthesia) is reported where analgesia has resulted from a lesion which has been proved to be confined to the medulla oblongata.

The central trigeminal or quintothalamic pathway.—Despite much careful investigation in the past on the anatomy of the central trigeminal pathway the accounts given in most modern anatomical and neurological writings are inadequate.

Hösel (1892) studied the brain of a woman, aged 52, who had suffered in earliest childhood a softening in the post-central region of one hemisphere. He found in the brain stem widespread degeneration of contralateral afferent tracts and sensory nuclei. The main sensory trigeminal nucleus was completely atrophied and there was atrophy in a small bundle of fibres in the pons lying between the ventral extremity of the superior cerebellar peduncle and the mesencephalic tract of the trigeminal nerve. As will be seen later the position of these atrophic fibres corresponds fairly closely with the dorsal quintothalamic tract of Wallenberg. Van Oordt (1896) examined the brain stem in a case where there was a softening in the medulla oblongata of some three months' duration. He was unable to trace any Wallerian degeneration but, from a study of the extent of the area of softening taken in conjunction with the clinical findings, he conjectured that the quintothalamic fibres crossed the raphe and ascended in the formatio reticularis of the opposite side.

Cajal (1895) was the first to give precise information on the position of the quintothalamic tract from the study of Golgi preparations in rabbits. He described two distinct quintothalamic tracts: (i) *a ventral tract*, consisting of crossed fibres, taking origin in the ganglion cells of the spinal nucleus and passing to the medial lemniscus of the opposite side, and (ii) *a dorsal tract*, consisting of uncrossed fibres, lying in the dorsolateral region of the formatio reticularis. Cajal later considerably modified this account of the quintothalamic tracts and his final views will be considered presently.

Wallenberg (1896), as already mentioned, placed lesions at various levels of the spinal tract of rabbits and studied the resulting Wallerian degeneration. He found that, following a destructive lesion in any part of the spinal tract and nucleus, degenerated fibres passed into the formatio reticularis of the opposite side just ventral to the hypoglossal nuclei. Traversing the substantia alba (in the region of the medial longitudinal bundles) they passed onwards to the formatio reticularis. Here they turned cephalad and ascended as a distinct tract to their termination in the ventral nucleus of the thalamus. As they were about to enter the thalamus they became blended with the fibres of the medial lemniscus. He also observed

degeneration in the ipsilateral internal arcuate fibres and in the contralateral medial lemniscus, but this he attributed to coincident damage to the cuneate nucleus. In 1900 he made further and more extensive studies. In addition to confirming his former observation on the dorsal quintothalamic tract he traced numerous degenerated fibres into the ventral part of the opposite medial lemniscus. He was unable to find any evidence of a dorsal quintothalamic tract if the lesion lay caudal to the cephalad limit of the decussation of the pyramids, but he admitted that there was a possibility of the presence of a ventral quintothalamic tract such as Cajal had described. However, he believed that the great majority of the degenerated fibres which passed in the internal arcuate fibres to the opposite medial lemniscus arose in the gracile and cuneate nuclei or, alternatively, that they represented ascending fibres in the postero-lateral tract which had originated in the upper cervical segments of the spinal cord. Cajal (1900) returned to the subject; described a short quintothalamic tract composed of both crossed and uncrossed fibres in the dorsal region of the formatio reticularis and suggested that its function was solely related to reflex medullary functions. He adopted this view because of the close association of this short tract with the nuclei of the facial, glossopharyngeal, vagal and hypoglossal nerves.

Van Gehuchten (1901) made further experimental studies on rabbits, and his method followed that which Wallenberg had used. He was careful to localize the lesions in the spinal tract and nucleus both above and below the cephalad limit of the decussation of the pyramids. He concluded that when the lesion involved the nucleus of the spinal tract below the cephalad limit of the decussation of the pyramids degeneration resulted in the ipsilateral internal arcuate fibres and in the contralateral medial lemniscus and, further, that degeneration did not occur in the formatio reticularis of the same or opposite side. If, on the other hand, the spinal nucleus were involved cephalad to the level of the decussation of the pyramids, fibre degeneration could be followed into the dorsal part of the formatio reticularis of the opposite side. Within the medulla oblongata the fila of the hypoglossal nerve divided this dorsal quintothalamic tract into two distinct bundles but, in the pons, the tract became compact and united and also moved laterally so that it lay within the curve of the emerging fibres of the facial nerve. In the mid-brain this dorsal quintothalamic tract lay dorsolateral to the medial longitudinal bundle and close to the junction of the formatio reticularis with the central grey matter. Finally, it passed into the ventral nucleus of the thalamus by way of the internal medullary lamina. Throughout its entire extent it was com-

pletely independent of the medial lemniscus. The only point of difference between Wallenberg and Van Gehuchten concerned the existence of a ventral quintothalamic tract, but it would appear that Van Gehuchten's views later underwent a change for, in the account of the trigeminal nerve in his textbook of nervous diseases, he (1906) described only a dorsal quintothalamic tract and made no mention at all of a ventral quintothalamic tract.

The foregoing summary of the quintothalamic tracts has been concerned almost entirely with observations drawn from experimental studies. What little information exists of the actual course of the quintothalamic tract in man concerns almost exclusively the central connections of the main sensory nucleus. Indeed in regard to that part of the quintothalamic tract which originates in the spinal nucleus there is, if we except the rather vague suggestions of Hösel and van Oordt, only one case which gives any accurate information and this was the case of occlusion by embolism of the left posterior inferior cerebellar artery from which Wallenberg (1895) had first deduced the segmental representation of the spinal tract of the trigeminal nerve. After some years this patient died and Wallenberg (1901) made an anatomical examination of the brain stem and confirmed the clinical diagnosis made six years before. The focus of old softening, which was some 5 mm. long, lay in the lateral part of the medulla oblongata and at the level of the opening of the central canal. Weigert preparations showed that the quintothalamic tract pursued the same course in man as in the rabbit; that is, it occupied the dorsal part of the formatio reticularis on the side opposite to the lesion. The value of this observation is doubtful. It has never been claimed that the quintothalamic tract is large and prominent and there must surely be some difficulty in its recognition in a "negative" stain such as Weigert's.

From this period onwards direct experimental and clinical reports on the anatomy of the quintothalamic tract are lacking. As will presently be seen this period marks a change in the conception of the anatomy of the quintothalamic pathway. Dejerine (1914) summarized the divergent opinions on the quintothalamic tract but he made one important modification. He stated that the bulbar portion of the ventral tract crossed to the *retro-olivary* region of the opposite side. This should be compared with the statements by Cajal and van Gehuchten that the ventral quintothalamic tract crossed the raphe near its ventral extremity and joined the medial lemniscus in the *inter-olivary* region.

Spiller (1908) had originally accepted Wallenberg's views on the position of the quintothalamic tract but, in a later publication (1915), he

stated: "The central tract of the trigeminal nerve in the medulla oblongata is believed by some to be situated a little in front of the hypoglossus nucleus; but it seems improbable that the fibres of temperature and pain from the face should occupy a tract distinct from that which contains the similar fibres from the trunk and limbs." In support of this opinion he cited Head and Holmes (1911) but these observers did not state precisely where the quintothalamic fibres joined with the main afferent tract for pain and temperature. From this time onwards, those who have mentioned the quintothalamic tract have all assumed that it lay in, or in close association with the spinothalamic tract. Stopford (1924) figured it in a position just medial to the spinothalamic tract and stated that there was ample evidence for assuming that the fibres taking origin in the spinal nucleus crossed the midline and formed a tract in the retro-olivary region and in close association with the spinothalamic tract.

It is probable that another factor has been effective in suggesting an anatomical association between the quintothalamic and spinothalamic tracts. This was the occasional occurrence of sensory loss on the contralateral face in cases of supposed posterior inferior cerebellar arterial occlusion. Now Stopford (1916) had shown that the substantia alba was not nourished by the posterior inferior cerebellar artery. Hence if the quintothalamic tract lay within the medial lemniscus, contralateral sensory loss on the face would not occur. Moreover, the assumption that the quintothalamic tract lay just medial to the spinothalamic tract received support from the frequent occurrence in cases of occlusion of the posterior inferior cerebellar artery of relative or absolute preservation of sensibility in the contralateral cervical region. Gordinier (1911) regarded the presence of a region of "cervical escape" as characteristic of the syndrome and argued that it resulted from the fact that the fibres conveying impulses for pain and temperature from the neck lay medial in the spinothalamic tract. Thus, if any part of the retro-olivary region escaped the ischæmic process, it was most likely to be that deep portion which contained the medial part of the spinothalamic tract, and the quintothalamic fibres, supposing them to lie most medial, would ordinarily escape destruction. It is obvious that the interpretation of this contralateral sensory loss on the face must affect the position we attribute to the quintothalamic tract. This question will be further discussed at a later stage.

Winkler (1921), in his study of the anatomy of the trigeminal nerve in the rabbit, gave a comprehensive account of the quintothalamic tract, but as he modified and amplified Cajal's original views, it is advisable to summarize his observations. He recognized a ventral and a dorsal quinto-

thalamic tract, both entirely crossed and, in contradistinction to van Gehuchten, he stated that the nucleus of the spinal tract gave origin to the ventral tract throughout its entire extent. He considered that, in the medulla oblongata at any rate, a small part of the dorsal quintothalamic tract lay within the substantia alba and medial to the fila of the hypoglossal nerve. In the pons this medial portion of the dorsal tract passed laterally to blend with the main part of the dorsal tract in the formatio reticularis. He found that the fibres destined to form the ventral quintothalamic tract were represented by the most ventrolateral of the internal arcuate fibres. They traversed the medial portion of the olivary nucleus and crossed the raphe in the interolivary region. Turning cephalad they ascended in the medial and ventral region of the medial lemniscus but, on reaching the pons, they became less compact. A fair number of these fibres passed towards the lateral part of the lemniscus. This suggested that the fibres of the ventral quintothalamic tract came, at length, into association with the spinothalamic tract. He believed that the ventral quintothalamic tract mediated pain and thermal impulses and, if his anatomical observations were correct, it follows that the pathway for pain and thermal sensibility from the face is not so anomalous, in a physiological sense, as would appear at first sight. Winkler found that the main sensory nucleus sent accessions of crossed fibres to both the dorsal and ventral quintothalamic tracts but the ventral tract received by far the larger addition. His observations on the short crossed and uncrossed reflex tracts, previously described only by Cajal, were complicated chiefly because he dealt at great length with the pathway for the corneal reflex. In rabbits he found that lesions in the caudal part of the spinal nucleus abolished the corneal reflex but only for a period of two or three weeks. In order to cause permanent loss of the corneal reflex he found it necessary to destroy the spinal tract in its most cephalad part. From this he deduced that, in the rabbit at any rate, there was a double afferent arc for the corneal reflex. Normally it would seem that the impulse travelled by way of the fibres of the ophthalmic nerve to the most caudal part of the spinal tract. From there it was relayed by the short reflex pathway to the nucleus of the facial nerve. However, there was in addition a second and much shorter afferent pathway open to the impulse but this more direct pathway was only used if the longer and more caudal pathway were closed.

Within more recent years no observations have been published bearing directly on the quintothalamic tract. A certain number of examples of vascular lesions of the brainstem (mostly reported as instances of occlusion of the posterior inferior cerebellar artery) have been described and these

were reviewed by Sheehan and Smyth (1937) in reporting two cases of occlusion of the vertebral artery. In all the reports, if it was mentioned at all, it was assumed that impulses underlying pain and thermal sensibility

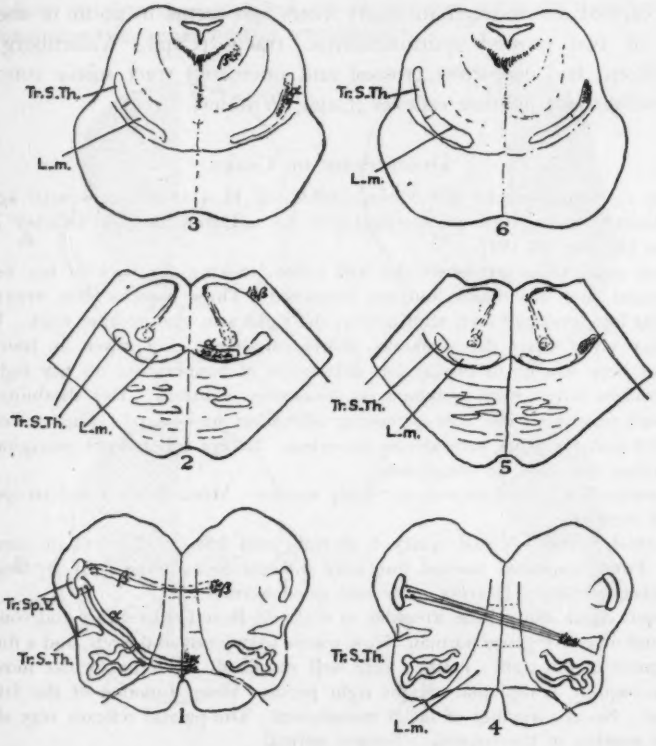

FIG. 1.—To illustrate the opposing views on the position of the quintothalamic tract. 1, 2, 3, the ventral and dorsal quintothalamic tracts according to Cajal, van Gehuchten and Winkler (Wallenberg recognized only the dorsal tract).

α the ventral quintothalamic tract.

β the dorsal quintothalamic tract.

4, 5, 6, the position of the quintothalamic tract according to Dejerine, Stopford, Elliot Smith and all recent English authors.

L.m. Medial lemniscus.
Tr. Sp. V. Spinal tract of the trigeminal nerve.
Tr. S. Th. Spinothalamic tract.

from the face crossed to the spinothalamic tract of the opposite side. Not a single case permitted a proper study of the secondary degeneration.

From the preceding review it will be apparent that it is

extremely difficult to convey a coherent account of the anatomical position and connections of the quintothalamic tracts since general agreement has never existed. The diagrams in fig. 1 give an outline of the most important hypotheses. Careful experimental and histological study carried out more than thirty years ago seems to point to the existence of two crossed quintothalamic tracts (Cajal, Wallenberg, van Gehuchten) and one short crossed and uncrossed tract solely concerned with bulbar and pontine reflexes (Cajal, Winkler).

Description of Cases.

Case 1. Syringomyelia and Syringobulbia.—C. H. (116/37), a woman aged 66, was admitted to the National Hospital (Dr. E. A. Carmichael) on October 12 and died on October 28, 1937.

Some eight years previously she had fallen, striking the back of her head on the ground, and was shaken but not concussed. Three months later weakness of the right leg developed and, after a year, the right arm also became weak. During the next seven years the weakness slowly increased. For three or four years she had been unable to distinguish differences of temperature on her right arm and painless burns were sustained on numerous occasions. Her disabilities had increased rapidly in the year preceding admission to hospital. She walked with difficulty and the arms were almost powerless. Except for a slight precipitancy of micturition she made no complaints.

Examination.—Well-nourished elderly woman. Mentally alert and co-operative. Speech normal.

Cranial Nerves.—Visual acuity 6/18 right and left. Fields full on confrontation. Fundi appeared normal but were difficult to examine fully by reason of lenticular opacities. Hearing, taste and smell normal.

Pupils equal, but a little irregular in outline. Reaction to direct and consensual light and on convergence normal. Slow, coarse nystagmus to the left, and a fine rapid nystagmus to the right; neither were well sustained. External ocular movements full, no squint or diplopia. Slight right ptosis. Motor function of the 5th nerve normal. No abnormality of facial movements. The palatal reflexes very sluggish. Severe wasting of the trapezii. Tongue normal.

Sensation of the face (fig. 2).—All forms of sensation were entirely normal on the left half of the face. On the right, marked disturbances were present, but only in the territories of the ophthalmic and maxillary nerves. There was almost total loss for prick and temperature in the territory of the ophthalmic nerve and moderate hypoalgesia and slight loss of thermal sensibility in the territory of the maxillary nerve. The appreciation of cold appeared to be more deficient than that of heat. The right corneal reflex was diminished; the left was brisk. There was marked hypoalgesia on the right palate and faucial arch. Tactile sensibility was normal on the right half of the face.

Motor and sensory functions.—Weakness and wasting of the upper limbs were severe. The lower limbs were moderately spastic; the right more than the left. The tendon-jerks, except for the triceps-jerk, were absent in the upper limbs. The right knee and ankle jerks were exaggerated and the right plantar response was extensor.

Appreciation of prick and temperature was grossly impaired in the arms and chest and, on the right, tactile anæsthesia was superadded. On the left leg and trunk, to as high as the 6th intercostal space, there was moderate loss for prick and temperature.

Postural sensibility and discrimination of two points simultaneously applied were lost in the right upper limb but only slightly impaired in the right lower limb. Examination of the other systems was negative.

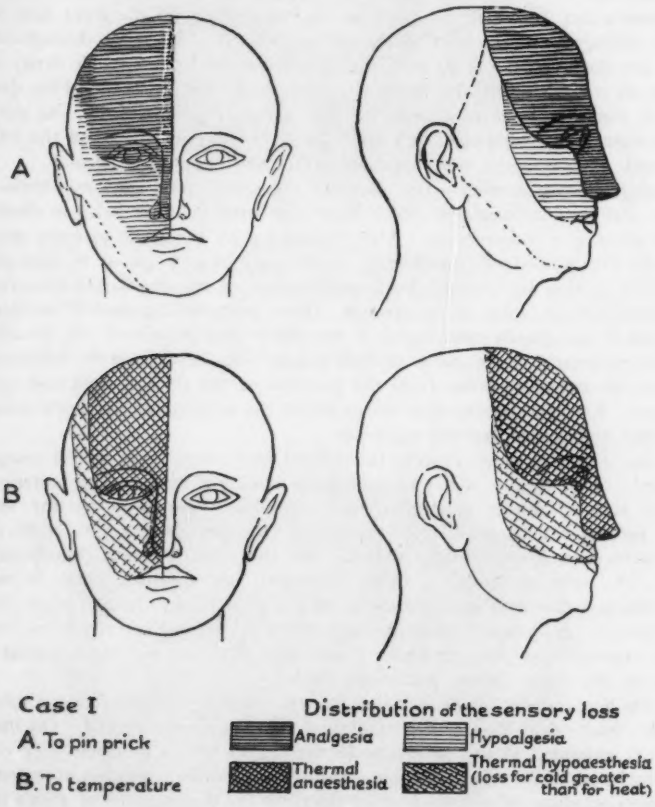

FIG. 2.—Chart of the sensory disturbances on the face in Case 1. Note the strict limitation of analgesia and thermanæsthesia to the entire territory of the right ophthalmic nerve. The area of partial sensory loss was equally limited within the territory of the right maxillary nerve.

The cerebrospinal fluid was under an initial pressure of 150 mm. of water and there was no evidence of spinal block. The fluid contained nine lymphocytes per c.c. and 0·100 grms. per cent. of protein. The Wassermann reaction was negative in blood and fluid.

To exclude the possibility of an intramedullary high cervical tumour 0·5 c.c. of lipiodol was injected into the cisterna magna on October 26. There were no immediate untoward results but twelve hours later she became speechless and unable to swallow. Examination did not disclose any gross alteration in the physical signs previously noted. Death occurred some 48 hours after the cisternal injection.

Post-mortem examination (Dr. J. G. Greenfield) within 12 hours of death. The convolutions of brain were atrophied, but the arteries at the base appeared normal (no thrombosis of vertebral or posterior inferior cerebellar arteries). The only other abnormality noted in the brain was a loss of bulk on the right side of the medulla oblongata at the level of the olivary nuclei. The cord, throughout the cervical and dorsal part, was the seat of a smoothly-lined syringomyelic cavity which occupied its centre, but in the thoracic region, from the 3rd to the 11th thoracic segments, reached the surface along the left posterior grey column. At the 12th thoracic segment it had shrunk to a small cavity in the grey matter on the left side of the cord. The posterior roots appeared rather more grey than normal.

Histological examination.—The medulla oblongata, pons and mid-brain were removed and cut into segments which were numbered in order so as to allow subsequent accurate reconstruction. After hardening in Weigert's primary mordant the blocks were embedded in celloidin. Serial sections were cut at 30 microns and every tenth section was stained by a modification of the Pal-Kultchitsky method and counterstained with alum-carmine. This procedure excluded an accurate estimation of the quality and degree of the gliosis and of minute cell changes but permitted thorough investigation of fibre tracts. The sections were mounted and numbered in ascending order from the junction of the cervical cord and medulla oblongata. It will suffice to describe in detail the sections of the brain-stem and of the first and second cervical segments.

At the second cervical segment the central grey matter was almost completely excavated. Only the tips of the anterior horns remained intact. The posterior grey columns and substantiæ gelatinosæ were completely destroyed by the syringomyelic process which, at this level, came to the periphery. The walls of the cavity were formed by dense glial tissue but the anterior white commissure was intact. The central canal was easily identified and appeared perfectly normal. Small vessels (arterioles) were numerous in the glial tissue which formed the wall of the cavity. All showed moderate adventitial thickening and, in a few, marked hyaline degeneration was present. There was pallor of the right lateral white column in the region of the pyramidal tract.

At the first cervical segment the cavity was smaller. On the left the substantia gelatinosa and spinal tract of the trigeminal nerve appeared normal. On the right the cavity extended to the periphery in the region of the posterior grey column. The spinal tract of the trigeminal nerve and the substantia gelatinosa were destroyed. The posterior white columns were normal except for the presence of gliosis in their deeper parts.

At the level of the decussation of the pyramids (fig. 3) (Sections 1 to 4), the cavity was smaller and almost limited to the right half of the oblongata. The central canal was preserved, although embedded in glial tissue and seemingly within the cavity. On the right the cavity extended to the periphery and destroyed entirely the spinal nucleus of the trigeminal nerve. At the dorsal lip of the cavity a small part of the spinal tract of the trigeminal nerve could be identified. A few transversely cut fibres, lying ventral to the ventral lip of the cavity, appeared to represent the posterior spinocerebellar tract.

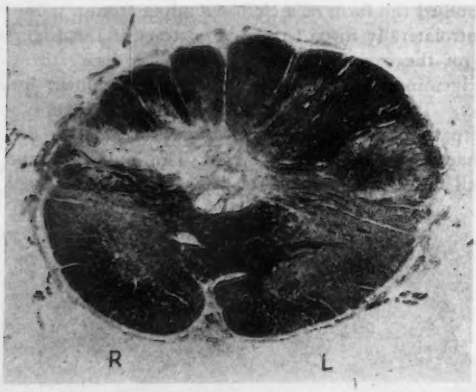

FIG. 3. *Case 1.*—Section at the level of the decussation of the pyramids. The cavity is limited to the right half of the medulla oblongata. The nucleus and spinal tract of the trigeminal nerve are destroyed and the right crossed pyramidal tract is partially invaded by gliosis. The fibres lying just ventral to the lateral extremity of the cavity probably represent the spinocerebellar tracts. Note the central canal lying within the cavity. Pal-Kultchitsky. × 5·5.

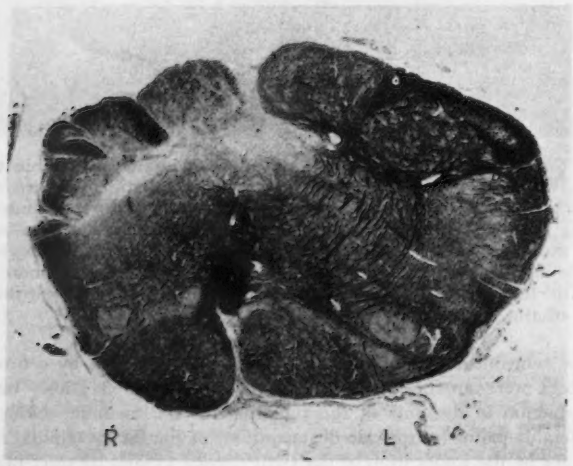

FIG. 4. *Case 1.*—Section (serial number 15) at the caudal level of the sensory decussation. The cavity has destroyed the nucleus of the spinal tract. The spinal tract itself is present but much reduced in bulk and unduly pale. There is a complete absence of internal arcuate fibres on this side and, on the opposite side (left), the medial lemniscus is wanting. There is slight pallor of the left pyramid. Pal-Kultchitsky. × 5·5.

At the level of the caudal extremity of the sensory decussation (fig. 4, Sections 9 to 15), the cavity assumed the form of a cleft extending from a point just dorsal to the central canal, ventrolaterally towards the spinal tract of the trigeminal nerve. The lateral extremity of the cavity had caused complete disorganization of the spinal nucleus of the trigeminal nerve and it reached the periphery immediately ventral to the spinal tract. The spinal tract was easily identified but it was much smaller than normal and pathologically pale. The gliosis surrounding the cavity was much less extensive than at more caudal levels. The nuclei of the posterior white columns were well developed and, on the left, heavily myelinated internal arcuate

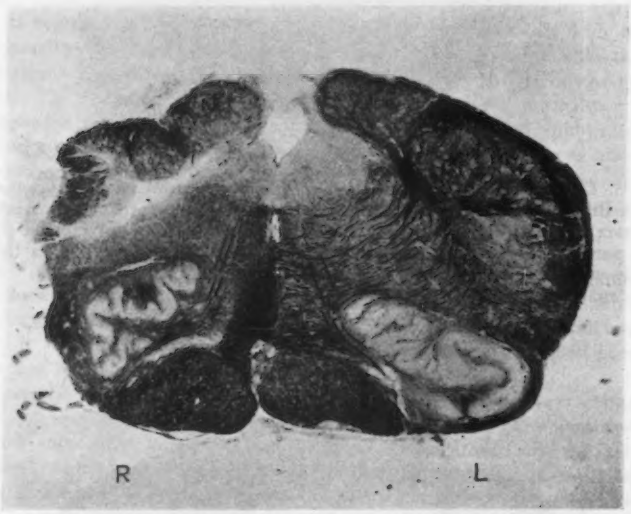

FIG. 5. *Case 1.*—Section (serial number 19) immediately caudal to the opening of the 4th ventricle. The cavity occupies a characteristic position. Medially it opens into the central canal dorsal to the dorsal vagal nucleus and laterally it touches the periphery ventral to the spinal tract of the trigeminal nerve. The nucleus of the spinal tract is destroyed by gliosis. Internal arcuate fibres are lacking on this side and, on the left, the medial lemniscus is wanting. There is a slight pallor of the left pyramid (retrograde degeneration). Note the shrinkage of the right half of the medulla oblongata. Pal-Kultchitsky. × 5·5.

fibres swept ventromedially towards the raphe. On the right, by contrast, internal arcuate fibres were absent. The cavitation and associated gliosis had led to a marked reduction in the bulk of the right half of the medulla oblongata. There was considerable pallor (retrograde degeneration) of the left pyramidal tract, readily accounted for by the implication of the right crossed pyramidal tract in the syringomyelic process.

At the cephalad extremity of the sensory decussation (fig. 5, Sections 16 to 21).—At Section 17 the central canal was nearing its termination and the olivary nuclei were well developed. The cavity was unchanged in shape. The spinal tract of the trigeminal nerve showed marked pallor and was still greatly reduced in bulk. The

nucleus of the spinal tract was completely disorganized. The nuclei of the posterior white columns were less in evidence and the descending root of the vestibular nerve was well defined. The tractus solitarius was well seen on the left, but on the right no trace of it was apparent. Internal arcuate fibres were a striking feature on the left as they swept in bold curves towards the opposite medial lemniscus. On the right internal arcuate fibres were absent and, in consequence, there was no trace of the left medial lemniscus. The medial longitudinal bundles and tectospinal tracts appeared normal. The hypoglossal and dorsal vagal nuclei were intact. The pyramidal tracts appeared normal.

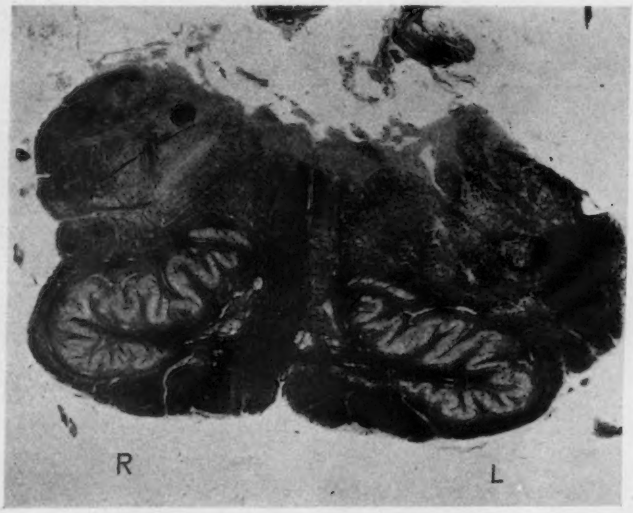

FIG. 6. *Case 1.*—Section (serial number 32) cephalad to the opening of the central canal. On the right the cavity is reduced to a mere slit and, for the first time, internal arcuate fibres can be seen traversing the formatio reticularis. Of the nuclei of the posterior white columns only the cuneate remains and even it is difficult to define. The descending vestibular root is prominent. A small cleft medial to the left tractus solitarius is present here and in a few adjacent sections. It probably represents a true syringobulbar process but does not appear to have had any clinical significance. Pal-Kultchitsky. × 5·5.

At Section 24 the central canal had opened into the 4th ventricle. The only important change in the syringomyelic process was a marked reduction in the extent of the cavity. Medially it opened into the 4th ventricle (at a point just dorsal to the dorsal vagal nucleus) but laterally it did not reach the periphery. Its lateral extremity fell within the nucleus of the spinal tract of the trigeminal nerve. The nucleus of the spinal tract was still much disorganized by gliosis but the spinal tract itself was merely reduced in bulk and abnormally pale. No internal arcuate fibres could be identified on the right but it is conceivable that a few might have found their way into the formatio reticularis by insinuation around the lateral extremity of the cavity. The gracile nucleus had almost ended and the cuneate nucleus was small and poorly delimited.

At Section 31 the cavity was greatly reduced in size and took the form of a narrow cleft lying in the plane of the emerging fibres of the glossopharyngeal nerve. Neither extremity came to the periphery and the surrounding gliosis (as judged by pallor) was small. The right spinal tract and nucleus of the trigeminal nerve appeared to be almost normal and it seemed as though fibres passed from the region of the nucleus towards the ventral part of the raphe crossing in their course the medial part of the olivary nucleus. The inferior cerebellar peduncles and the medial and spinal vestibular nuclei were well developed. It was impossible to distinguish the cuneate nucleus as a distinct structure. By Section 32 the cavity

FIG. 7. *Case 1.*—Section (serial number 44) at the level of the cephalad half of the open part of the medulla oblongata. A fair number of ascending fibres are now evident, and, on the whole, they occupy the ventromedial region of the medial lemniscus. This section is far cephalad to the cavity and the appearances of the left medial lemniscus are in marked contrast with those seen in fig. 6. Pal-Kultchitsky. ×7·5.

had further diminished in size and in the next section it had disappeared. In sections immediately cephalad to this level its former position was represented by a band of slight pallor in the plane of the glossopharyngeal and vagal nerve roots. The most cephalad level at which the cavity was encountered corresponded with the most cephalad portions of the cuneate nuclei (fig. 6).

Sections 33 to 59.—Throughout the cephalad half of the open portion of the medulla oblongata the fibre tracts and nuclear masses appeared normal excepting that the left medial lemniscus remained rudimentary. It was observed that, as the sections were traced cephalad, there was a progressive increase in the fibres in the left medial lemniscus (fig. 7). The probable source of these fibres will be discussed

later, but for the present it should be noted that the nuclei of the posterior white columns had almost ended before the cavity had terminated. Consequently whatever the source of the progressively increasing fibres in the left medial lemniscus they clearly could not have originated as internal arcuate fibres from the nuclei of the posterior white columns, and for this reason their position and course merit close scrutiny. In the most caudal sections in which they could be certainly identified they occupied a narrow zone in the most ventral and medial part of the lemniscus and they were closely applied against the raphe. As the medulla oblongata was traced cephalad these fibres, as has been noted, increased in number but they continued to preserve their medial and ventral position. A few transversely cut fibres were, it is true, seen throughout the whole area of the left medial lemniscus, but the more definite and compact bundle in the ventromedial part stood out quite conspicuously at all levels of the medulla oblongata. In Sections 58 and 59, which corresponded with the junction of pons and medulla oblongata, the olivary nuclei became rapidly contracted and the right medial lemniscus expanded laterally. Simultaneously the fibres in the left medial lemniscus scattered although still maintaining their ventral position. This change was well seen in Section 62, where the site of the left lemniscus was evenly stippled with fibres. Lateral to this area of stippling lay the well-defined spinothalamic tract. Cephalad to the level of the facial nuclei the remnant of the left medial lemniscus underwent a further change. The fibres were still rather diffusely scattered but they seemed to be extending in a lateral direction and, at the level of the main sensory nucleus of the trigeminal nerve, it was impossible to distinguish them from the fibres of the spinothalamic tract. A close study of sections at this level gave the impression that the medial lemnisci received an accession of fibres at the level of, or immediately cephalad to, the main sensory nucleus of the trigeminal nerve. In the cephalad half of the pons and throughout the mid-brain the degenerated left medial lemniscus was easily followed. The right medial lemniscus was closely applied to the lateral margin of the red nucleus. In the corresponding region on the left side there was merely a rather diffuse pallor. In the most cephalad section in the series (at the level of the ventral nucleus of the thalamus) the picture was substantially similar but the pallor was too diffuse to allow of exact localization.

The Correlation of the Post-Mortem and Clinical Observations.

The motor and sensory signs in the trunk and limbs were such as are commonly found in syringomyelia. Over the chest and upper limbs the analgesia and thermanæsthesia could be attributed to the direct implication of the central grey matter of the spinal cord. The tactile anæsthesia on the right might be attributed to extension of cavitation into the right posterior grey columns so as to bring about destruction of the most medial fibres in the root entry zone. However, the virtual section of the posterior white columns on this side (by cavitation in the medulla oblongata), is perhaps more likely. The analgesia and thermanæsthesia on the left trunk and leg cannot be elucidated in this way for the cavitation did not extend into the lumbar segments of the spinal cord. They probably

depended on some degree of involvement of the right spinothalamic tract. We know, indeed, that the right lateral column was affected, as evidenced by the spastic weakness of the right leg as well as by the retrograde pallor of the pyramidal tract. The weakness and wasting of the upper limbs were clearly secondary to partial destruction of the cells of the anterior grey columns in the cervical region of the spinal cord. In the medulla oblongata and pons the clinical signs were in accord with the histological changes seen. From above the level of the 2nd cervical segment of the spinal cord the cavity was limited to the right and it extended cephalad as high as the caudal part of the 4th ventricle. In its caudal half the cavity had caused a severe disorganization of the spinal tract of the trigeminal nerve and a complete destruction of the spinal nucleus. In its cephalad half the damage done by the cavity to the spinal tract and nucleus was less severe but at all levels, except those just caudal to the cephalad extremity of the cavity, the affection of the spinal nucleus was very definite. Furthermore, the cavity had effectively cut the path of all the internal arcuate fibres and, in consequence, the left medial lemniscus was absent.

The full interpretation of these observations, particularly in so far as they shed light on the segmental representation of the spinal tract of the trigeminal nerve, will be discussed more fully at a later stage. For the present the analgesia and thermanæsthesia in the territory of the right ophthalmic nerve will be attributed to the destruction of the most caudal part of the spinal tract of the trigeminal nerve. Similarly the hypoalgesia and thermal hypoæsthesia in the territory of the right maxillary nerve will be attributed to the *partial* destruction of the spinal tract of the trigeminal nerve in levels of the medulla oblongata towards the cephalad extremity of the cavitation.

The nystagmus, which is such a constant sign in syringobulbia is usually attributed to an affection of the descending root of the vestibular nerve, or of its central connections. This would be an adequate attribution in the present case.

Case 2.—*Thrombotic occlusion of the right posterior inferior cerebellar artery.*—A. B., a man aged 48, was admitted to a Leeds Hospital (Dr. Hugh Garland) on August 23 and died on September 4, 1936.

On August 19, 1936, the patient, who had previously enjoyed good health, was seized with sudden and severe giddiness, inability to swallow and loss of voice. In addition he complained of double vision and marked clumsiness in the use of his right arm and leg. When admitted to hospital four days after the onset of his illness he was drowsy and obviously gravely ill. Throughout his illness he was troubled by severe and persistent hiccup.

Examination.—The pupils were equal and regular in outline, their reactions were normal. There was diplopia (but no manifest strabismus) on looking down and particularly on looking to the right. There was coarse nystagmus on looking to the right and a more rapid and fine nystagmus to the left. There was no facial asymmetry or weakness. There was marked paresis of the right palate, the uvula being drawn up to the left on attempted phonation. There was aphonia and severe dysphagia. The function of taste was not examined.

Sensation on the face.—The following facts were established. There was a total analgesia on the right side of the face accurately confined to the territory of the trigeminal nerve. The right corneal reflex was absent. Thermal sensibility was not examined. There was an absence of any trace of sensory loss on the left half of the face and the left corneal reflex was active. Tactile sensibility was probably normal but as this observation was not recorded in writing it has not the validity of the other observations.

On the trunk and limbs there was a gross ataxy and hypotonia of the right arm and leg together with a slight degree of muscular weakness. The right plantar response was feebly extensor; the left was flexor. There was analgesia on the whole of the left half of the body excluding the territory of the left trigeminal nerve. The upper border of this sensory loss coincided with the posterior border of the trigeminal area. The patient died sixteen days after the onset of his symptoms.

Post-mortem examination was carried out by Dr. Polson of Leeds who found a thrombus occluding the right posterior inferior cerebellar artery. He very kindly preserved the brain-stem intact and sent it to the Pathological Laboratory of the National Hospital, Queen Square.

Histological examination.—Portions of the medulla oblongata and pons, after fixation in formol saline, were put into Weigert's primary mordant preliminary to the application of myelin sheath staining. Representative portions of the medulla oblongata and pons were reserved for examination by the Marchi technique. By these means sections were obtained from all levels of the medulla oblongata and pons and, though no attempt was made to secure strictly serial sections, there was little difficulty in forming an accurate estimation of the extent of the lesion and of the position of the Wallerian degeneration.

The nature and extent of the lesion.—The most caudal sections passed through the junction of medulla oblongata and cervical spinal cord at, approximately, the most caudal level of the decussation of the pyramids. In the first two sections the appearances were normal. By Section 3 it was apparent that the fibres of the right posterior spinocerebellar tract were abnormal. In cross section the myelin sheaths were vacuolated and reminiscent of the early changes seen in subacute combined degeneration of the cord and in certain cases of contusion of the cord. This appearance was of interest in that it suggested an anoxæmic effect on the nutrition of myelin, but the subject cannot be further pursued here. At the caudal level of the sensory decussation true ischæmic softening was first observed. It occupied a small area in the position of the posterior spinocerebellar and spinothalamic tracts. The spinal tract and nucleus of the trigeminal nerve were partially affected. Traced cephalad the lesion rapidly increased in size and at the opening of the central canal (fig. 8, Section 17) it assumed the form of an irregularly quadrilateral plate, and occupied the greater part of the right formatio reticularis. At this level it involved the cephalad portion of the gracile and cuneate nuclei, the anterior and posterior spinocerebellar tracts, the spinal tract and nucleus of the trigeminal nerve, the spino-

thalamic and rubrospinal tracts, the lateral half of the dorsal part of the olivary nucleus and the lateral half of the dorsal accessory olivary nucleus. The central grey matter, the descending root of the vestibular nerve, the medial lemniscus, the pyramidal tract, the medial and ventral parts of the olivary nucleus and a portion of the formatio reticularis adjacent to the substantia alba were all entirely spared. The dorsomedial tip of the area of softening touched, but did not invade, the tractus solitarius. In more cephalad sections the extent of the lesion remained fairly constant or, if anything, increased. At the mid-level of the open part of the medulla oblongata (Section 31) the lesion was beginning to diminish in size. The right inferior cerebellar peduncle and the spinal tract and nucleus of the trigeminal

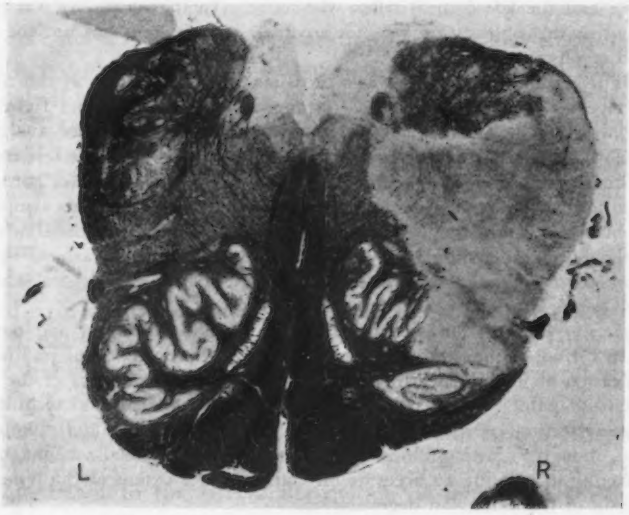

FIG. 8. *Case 2.*—Section immediately cephalad to the opening of the central canal. The focus of ischæmic softening occupies a large part of the right formatio reticularis and implicates the cuneate nucleus, the spinal nucleus and tract of the trigeminal nerve, the nucleus ambiguous, the spinocerebellar tracts, the spinothalamic tract and the lateral half of the dorsal part of the olivary nucleus. Pal-Kultchitsky. ×5·5.

nerve were totally within the lesion. The whole of the olivary nucleus and the immediate retro-olivary region were now unaffected. In more cephalad sections the lesion grew rapidly smaller and just caudal to the uppermost fila of the glossopharyngeal nerve it occupied a small area corresponding to the position of the spinal tract of the trigeminal nerve (fig. 9, Section 34). More cephalad sections had not been stained by the Pal-Kultchitsky method but, from the Marchi preparations, it was evident that the most cephalad levels of the medulla oblongata were entirely free from softening. Sections stained by the Pal-Kultchitsky method, of all levels of the pons, showed a perfectly normal appearance. There was no trace of either ischæmic softening or secondary degeneration.

The secondary degeneration of tracts demonstrated by the Marchi technique.—In sections passing through the caudal poles of the olivary nuclei the lesion was seen to occupy a wedge-shaped area interposed between the right olivary and cuneate nuclei. The softening partially implicated the spinal tract and nucleus of the trigeminal nerve. From the margin of the lesion degenerated fibres passed in broad curves towards the ventral half of the raphe. Many of these certainly took origin in the cells of the cuneate nucleus but it seemed probable that the most ventrolateral of these internal arcuate fibres originated in the neighbourhood of the nucleus of the spinal tract. Having crossed the raphe it was quite clear that

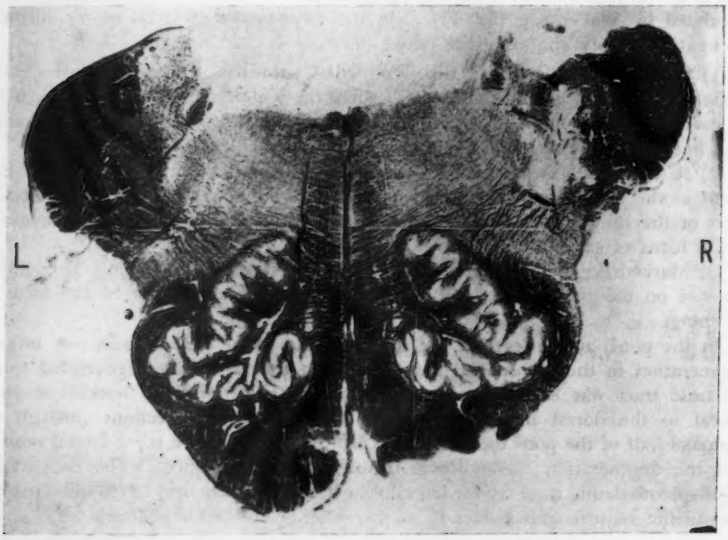

FIG. 9. *Case 2.*—Section close to the most cephalad level of the medulla oblongata. The focus of ischæmic softening in the right formatio reticularis has now contracted into a small area which occupies the position of nucleus of the spinal tract of the trigeminal nerve. Pal-Kultchitsky. × 5·5.

these degenerated fibres were taking part in the formation of the medial lemniscus. The stippling in the left medial lemniscus thus produced was most dense in the ventral third of the substantia alba. Degenerated fibres were relatively scanty in the dorsal two-thirds of the lemniscus (fig. 10). It was noted as a fact of importance that there was a total absence of degeneration throughout the whole of the formatio reticularis of the left side of the medulla oblongata. In sections through the caudal half of the open part of the medulla oblongata the appearances confirmed and amplified the observations made at more caudal levels. The extent of the lesion was here at its maximum. The nuclei of the posterior white columns had almost ended but, on the right, a considerable number of degenerated internal arcuate fibres was still seen. The most ventrolateral of these fibres traversed the medial part of the olivary nucleus, crossed the raphe almost at right angles,

and finally joined the left medial lemniscus. The degeneration in the left medial lemniscus was by now very intense but it was limited to the ventral third of the substantia alba and, on the whole, it was most dense in the medial half of the lemniscus. Examination of the formatio reticularis on the left, and in particular of the region occupied by the spinothalamic tract, again showed a complete absence of secondary degeneration. This was equally true of the dorsomedial part of the left formatio reticularis, in which region Wallenberg had placed the dorsal quinto-thalamic tract. Two or three fine degenerated fibres were, it is true, seen in this region. Their significance will be referred to later. For the present it is sufficient to point out that they in no way approximated to a definite tract in the sense postulated by Wallenberg (fig. 11). In the most cephalad levels of the medulla oblongata the only abnormalities noted were :—

(1) Intense degeneration of the left medial lemniscus. The increased density of the degenerated fibres in the medial half of the lemniscus was still very apparent. At most a few degenerated fibres were seen scattered throughout the substantia alba, but this sparse degeneration was quantitatively equal on both sides.

(2) A moderately well-defined bundle of degenerated fibres immediately subjacent to the right antero-lateral sulcus. This certainly represented the ascending fibres of the spinothalamic tract which, at a more caudal level, had been involved in the focus of softening.

(3) Marked degeneration in the right interior cerebellar peduncle. This clearly followed on the implication of the posterior spinocerebellar tract in the focus of softening.

In the pons, at the level of the nuclei of the facial nerves, there was intense degeneration in the left medial lemniscus. On the right, the degenerated spinothalamic tract was easily identified. It formed a rather loose bundle of fibres lateral to the dorsal nucleus of the trapezoid body. In sections through the cephalad half of the pons the left medial lemniscus occupied a more lateral position and the degeneration was uniform throughout its substance. The degenerated right spinothalamic tract lay far laterally in the tegmentum and in close approximation to the ventrolateral convexity of the superior cerebellar peduncle.

The Correlation of the Post Mortem and Clinical Observations.

This case is a typical example of the syndrome of occlusion of the posterior inferior cerebellar artery. The hypotonia and ataxy of the right arm and leg were attributable to destruction of the ipsilateral spinocerebellar tracts and by the scarcely less severe affection of the ipsilateral internal arcuate fibres. The contralateral analgesia on the trunk and limbs resulted from implication of the right spinothalamic tract. In this case the territory supplied by the posterior inferior cerebellar artery was maximum and the area of ischæmic softening extended into the formatio reticularis to the middle of the dorsal border of the olivary nucleus. The presence of an extensor plantar response on the right is perhaps rather difficult to account for. Possibly the right crossed pyramidal tract suffered some nutritional disturbance. That the right lateral white

FIG. 10. *Case* 2.—Section towards the caudal part of the sensory decussation. Degenerated internal arcuate fibres pass from the region of the lesion towards the raphe. Ascending degenerated fibres are present in the opposite medial lemniscus. There is a complete absence of tract degeneration in the dorso-medial regions of the formatio reticularis. None of the degenerated fibres passes to the region of the spinothalamic tract. Marchi-Busch. × 8·5.

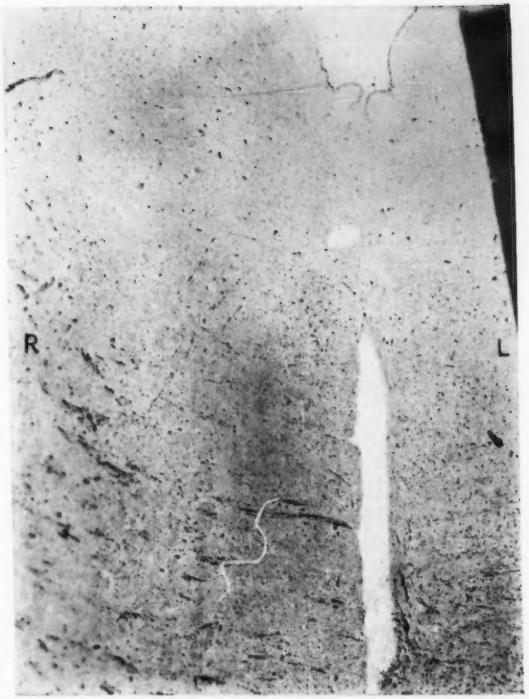

FIG. 11. *Case* 2.—Section at the level of the opening of the central canal. Towards the bottom of the plate the course of the degenerated internal arcuate fibres is well seen. Note the manner in which they bear ventralward after crossing the raphe. There is no evidence of a dorsal quintothalamic tract but a few fine degenerated fibres lying just ventrolateral to the position of the right hypoglossal nucleus occupy the position assigned to the reflex medullary pathway of the trigeminal nerve (Cajal). Marchi-Busch. × 26.

column was affected was proved by the definite vacuolation observed in the region of the spinocerebellar tracts. The aphonia, dysphagia and right palatal palsy were explained by the destruction of the ipsilateral nucleus ambiguous. The causation of the nystagmus and diplopia is by no means clear. Both have frequently been reported in cases of this nature and in which the pons was intact. They probably result from an acute lesion which implicates the spinal vestibular tract or which cuts its connections with the medial longitudinal bundles. The chief interest in this case lies in the help that it affords in the localization of the quintothalamic tract and, in lesser degree, in an understanding of the segmental representation of the spinal tract and nucleus of the trigeminal nerve. For the present it is sufficient to reiterate that, neither caudally nor cephalad in the medulla oblongata, was there the least evidence of a dorsal quintothalamic tract or of an anatomical association of the spinothalamic and quintothalamic tracts.

Case 3.—Operative Section of the Spinal Tract of the Trigeminal Nerve for the Relief of Trigeminal Neuralgia.—C. D., a man, aged 39, was admitted to the National Hospital, Queen Square (Dr. E. A. Carmichael), on February 22, 1938. He complained of brief but extremely severe paroxysms of pain in the right upper lip and cheek which had occurred on and off for ten years. The history which he gave was typical of severe trigeminal neuralgia. The paroxysms had always been strictly confined within the territory of the right maxillary nerve. The usual exciting stimuli were all effective in provoking volleys of pain and, at the time of his admission, he was in a state of ketosis as a result of a fear of eating. In 1934, and again in 1936, alcohol injections had been made into the right trigeminal ganglion, but on each occasion he had only a few months' relief.

Examination.—In the territory of the right trigeminal nerve there was a very slight hypoalgesia ; a residual effect of the alcohol injections. Other forms of sensibility were intact. The corneal reflexes were equal and brisk. Taste was normal. There was no other abnormality of the cranial nerves. Motor and sensory function were normal. The cardiovascular and respiratory systems were healthy. Radiograms of the skull showed changes suggestive of early Paget's Disease, the vault of the skull being particularly affected. Because of this it was felt that the temporal approach to the sensory root would be fraught with the risk of grave hæmorrhage and it was decided to attempt a section of the spinal tract. As a preliminary the state of sensibility in both trigeminal areas was carefully re-examined in order that there would be a proper standard for the assessment of the post-operative changes. Re-testing showed that apart from an extremely slight hypoalgesia in the whole of the right trigeminal area, trigeminal sensibility was normal. The lightest contacts with cotton wool were equally appreciated on both sides of the face. Two-point discrimination at a separation of 0·5 mm. was uniformly accurate on the lips and cheeks. The threshold for pressure pain was determined with the algometer. It was found that pressures of seven to nine pounds caused pain over the forehead, cheek and chin on both sides. Care was taken to ensure that the head was firmly supported whilst the pressure was applied.

Operation (Mr. Harvey Jackson), March 17, 1938.—The cerebellum and medulla oblongata were exposed by removing the overlying occipital bone and the arch of the atlas. The most caudal rootlet of the right vagus was taken as the guide and immediately caudal to this a horizontal incision was made with a guarded tenotomy knife into the lateral aspect of the oblongata to a depth of 3·5 mm. The knife, was inserted ventrally and drawn backwards till it emerged just ventral to the inferior cerebellar peduncle. Later the same day a cursory examination showed that there was analgesia of the right ophthalmic and maxillary territories with abolition of the right corneal reflex. Touch was unaffected. The general condition was satisfactory. Convalescence was uneventful. At no time was there any indication of severe cerebellar disturbance or of sensory disturbance on the trunk or limbs.

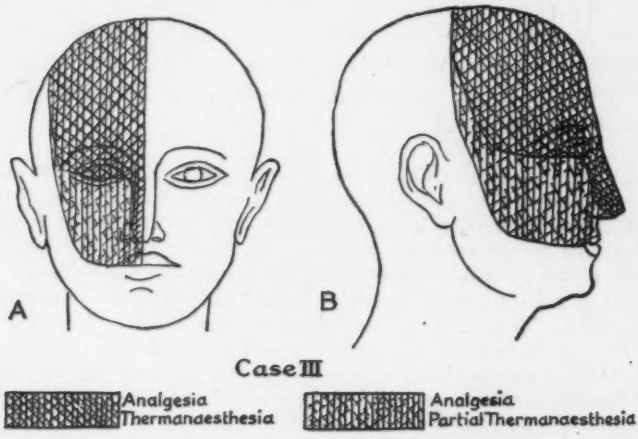

FIG. 12.—Distribution of sensory loss in the territories of the right ophthalmic and maxillary nerves.

Post-operative condition on March 31, 1938.—At rest in bed the only trace of cerebellar disturbance was a relative slowness of alternating movements of the right arm and leg. However, the gait was definitely abnormal. The patient veered towards the right and was slow and clumsy in turning. Apart from these signs the only abnormalities present were those referable to the right trigeminal nerve. The functions of the left trigeminal nerve were entirely normal. The diagrams (fig. 12) indicate the sensory loss. Analgesia was complete in the territories of the ophthalmic and maxillary nerves and the corneal reflex was absent. The loss of thermal sensibility was complete in the area of the ophthalmic nerve and all temperatures evoked a neutral sensation. Over the territory of the maxillary nerve thermal discrimination was merely blunted. Slight inequalities in temperature were confused. Hot and cold were equally less well perceived. The inner aspect of the upper lip, the right half of the palate and the right faucial arch were anâlgesic. Taste and common sensation on the tongue were unaffected. *Pressure pain* was absent on the right forehead and cheek provided the head was firmly supported.

Whereas on the corresponding points on the left side the threshold for pain was from 7 to 9 pounds, on the right pressure of 20 pounds failed to arouse discomfort or pain. In testing for pressure pain in the cheek the examiner's finger was inserted into the patient's mouth to make counter pressure and to exclude deformation of the tissues by the thrust of the algometer. *Touch* was perfectly intact over the analgesic areas. Contacts with a von Frey's hair (2 grammes per sq. mm.) were equally well perceived on the two sides of the face. The patient himself stated that touching the analgesic areas aroused no sensation of tickle. *Discrimination of two points* simultaneously applied was as good on the analgesic area as on the sound side. A separation of 0·5 cm. was correctly perceived on both sides of the upper lip and along the sides of the nose. His symptoms were entirely relieved and there was a complete absence of subjective numbness and paræsthesia. This was in marked contrast with the state of many patients following section of the sensory root of the trigeminal nerve. It is interesting to note that headache, which lasted for about a week after the operation, was strictly confined to the left half of the scalp. This fact was spontaneously remarked on by the patient.

Summary.

Operative section of the spinal tract of the trigeminal nerve at the level of the most caudal rootlet of the vagus was successfully performed without injury to the spinothalamic tract and with only (presumably) slight damage to the inferior cerebellar peduncle. There resulted an analgesia in the territories of the ipsilateral ophthalmic and maxillary nerves and loss of the corneal reflex. Thermal sensibility was lost over the ophthalmic territory and blunted over the territory of the maxillary nerve. Pressure pain was abolished on the analgesic side on the forehead, over the maxilla and on the cheek. Touch and discrimination of two points simultaneously applied were entirely unaffected.

Discussion of Results.

Before any conclusions can be drawn from the cases whose clinical histories and pathological findings have just been recorded it is necessary to show that the cases were intrinsically suitable for study and that the pathological examinations were sufficiently full. The first patient (Case 1) was repeatedly examined by independent observers and the observations recorded were those, and only those, on which there was general agreement. It was unfortunate that deep sensibility of the face in two of the patients was not examined, but this omission in no way invalidates the assessment of other forms of sensibility. It is also regrettable that in Case 2 tactile and thermal sensibility were not accurately determined, but it will be proper to use this case to explain the distribution of the analgesia and the probable pathway of the bulbar portion of the quintothalamic tract.

With regard to the intrinsic suitability of the cases it will be conceded that, in the human subject, there are only two disease processes which should ordinarily be used for exact anatomical studies. The common systemic degenerations, infections and tumour formations are generally very poorly circumscribed. In contrast, syringobulbia and limited vascular lesions are much more sharply defined and in the past both have given information of great value. Of the two, circumscribed vascular lesions have, in the past, proved the more valuable, despite the objections which have been raised on the grounds that the initial disturbances following acute vascular lesions are necessarily in excess of what would have been expected from the extent of the lesion. This objection can be overcome, in great measure, if attention is confined to those disturbances which experience has shown to remain permanent and unaltered. Thus, in occlusion of the posterior inferior cerebellar artery it is commonly found that in the course of time the hemiataxy and disturbed sensibility in the trunk and limbs slowly recede or entirely disappear. It is otherwise with the trigeminal analgesia. A reference to the published case reports of patients surviving for years occlusion of the posterior inferior cerebellar artery shows that there is rarely any shrinkage of this analgesic area.

Syringobulbia may yield valuable information, but only in certain instances and when the histological examination has been thorough. It is certain that failure to satisfy these requirements is responsible in no small measure for the confusion which besets the problems presented by the trigeminal nerve. It must be evident that it is not possible to draw reliable conclusions from cases of syringobulbia in which the cavity is interrupted by bridges of normal tissue. The risk of error becomes even greater when the cavity destroys only a part of the spinal nucleus of the trigeminal nerve and when the interpretation of the distribution of the sensory loss is made to rest on the supposed interruption of the second sensory neurone.

The three cases here reported appear suitable for study. They presented clear-cut lesions and the histopathological studies were made at all levels throughout the extent of the lesions.

The segmental representation of the spinal tract and nucleus of the trigeminal nerve.—The material provided by these cases lends strong support to the view that the representation within the spinal tract and nucleus of the trigeminal nerve is in terms of the peripheral divisions of the nerve and in an order which is the inverse of the peripheral distribution. In Case 1 there was, during life, a well-defined sensory loss on the

right side of the face. It is important to note that the medial border of the area of analgesia and thermal anæsthesia extended along the midline of the nose and from there passed upwards to the vertex. Reference to fig. 2 makes this clear and shows also the hypoalgesia and partial thermanæsthesia in the territory of the right maxillary nerve. The crucial observations in this case were the accurate correspondence of the areas of sensory loss within the territories of the ophthalmic and maxillary nerves and the sharp medial border of the area of sensory loss at the midline of the face. Furthermore, it should be noted that the sensory loss was most intense in the territory of the ophthalmic nerve and only partial in the territory of the maxillary nerve.

Pathologically a cavity was found in the right half of the caudal third of the medulla oblongata and destroying the more caudal part of the spinal tract and nucleus of the trigeminal nerve.

The clinical and histological observations in this case may be harmonized on the assumption that all the ophthalmic fibres descend to the most caudal part of the spinal tract of the trigeminal nerve and there end in synaptic relation with the most caudal part of the nucleus of the spinal tract. The maxillary fibres also descend in the spinal tract but they end in relation to an intermediate part of the nucleus of the spinal tract. The partial involvement of these maxillary fibres is in keeping with the partial nature of the sensory loss in the territory of the maxillary nerve and it is explicable by the incomplete nature of the lesion of the nucleus of the spinal tract towards the more cephalad extremity of the cavity. The complete escape of the mandibular fibres shows that they terminate within the nucleus of the spinal tract cephalad to the most cephalad limit of the cavity. The clinical and histological findings in Case 2 are in conformity with these views. Here there was a total analgesia strictly limited to the territory of the right trigeminal nerve. Histological examination showed that a focus of ischæmic softening had destroyed the spinal tract and its nucleus, but, in this instance, they were destroyed at a more cephalad level than in Case 1. Since it was plain that the most cephalad level of the medulla oblongata was quite unaffected by the lesion and it follows that the mandibular fibres must end in the nucleus of the spinal tract at some level between the opening of the central canal and the most cephalad level of the medulla oblongata. These limits are wide and there is nothing in either of these cases to indicate whether the mandibular fibres end diffusely throughout the very considerable length set by these limits or more discretely towards its caudal or cephalad limits. The results obtained by Sjöqvist (1938) appear to settle this problem and it appears

highly probable that the mandibular fibres in the spinal tract end immediately caudal to the middle of the open part of the medulla oblongata.

It is important to note the distribution of the thermanæsthesia in Case 3. The area of total thermanæsthesia was strictly limited to the territory of the ophthalmic nerve. Similarly the area of partial thermanæsthesia was accurately confined to the territory of the maxillary nerve. However, analgesia was complete in the maxillary territory and this suggests that the segment of the nucleus of the spinal tract concerned with thermal sensibility lies at a level cephalad to that for pain. It is plain that the distribution and degree of the defect of thermal sensibility in this case can only be explained on the assumption that its representation in the spinal tract is in terms of the peripheral distribution of the nerve and that those fibres of the ophthalmic nerve, which mediate thermal impulses, descend further caudally than similar fibres from the maxillary nerve. As in Cases 1 and 2, the sensory disturbances in this case cannot be reconciled with a theory which postulates a segmental representation in the spinal tract in terms of concentric zones converging towards the nose and mouth.

Direct histological examination of the nucleus of the spinal tract of the trigeminal nerve cannot, of course, be expected to give much direct evidence bearing on the segmental representation of the spinal tract and nucleus. The significance of the variations in the morphology of the nucleus of the spinal tract of the trigeminal nerve is obscure but it is permissible to suspect that they subserve a functional differentiation. It may be that the fibres of all three components of the trigeminal nerve end in relation to that part of the nucleus of the spinal tract which lies in the caudal third of the medulla oblongata and whose structure is uniform with that of the substantia gelatinosa. Alternatively only the fibres of the ophthalmic and maxillary nerves may pass to this caudal portion of the nucleus, leaving the mandibular fibres to make synaptic relation with a part or the whole of the cephalad two-thirds of the nucleus of the spinal tract. Either hypothesis would be in harmony with the clinical and pathological findings in these cases but, on the whole, the second would appear the more reasonable and, furthermore, it is in agreement with Sjöqvist's observations.

At this point it is instructive to refer to the distribution of sensory loss on the face in the reported cases of the retro-olivary syndrome of vascular origin. Such a study throws further light on the probable nature of the segmental representation in the spinal tract and nucleus of the trigeminal nerve. In a recent paper Sheehan and Smyth (1937) reviewed all the

examples of this syndrome published since Stopford's critical analysis in 1924. In three-quarters of the cases reviewed the trigeminal sensory loss was on the side of the lesion and in the great majority the analgesia affected all three branches of the trigeminal nerve but, when the sensory loss was less extensive, it was invariably greatest in the territory of the ophthalmic nerve or in the territories of the ophthalmic and maxillary nerves. Moreover, the sensory loss invariably extended to the mid-line of the face and was exclusively in terms of the three divisions of the trigeminal nerve. Where only a part of the trigeminal area was affected the territory of the ophthalmic nerve was the most likely to suffer, and, if any part of the trigeminal area escaped, then the mandibular territory was the area showing a state of normal sensibility. It has been shown that vascular lesions of the lateral area of the medulla oblongata, thanks to the variability in the vascular supply, may involve the spinal tract and nucleus of the trigeminal nerve at varying levels. Such lesions perform remarkably clear-cut experimental sections of the spinal tract and give thereby information of the greatest value. From the resulting sensory disturbances the conclusion is inescapable that the peripheral divisions of the trigeminal nerve are represented within the spinal tract in such a manner that the ophthalmic fibres terminate most caudally, the mandibular fibres most cephalad, whilst the maxillary fibres end at an intermediate level.

The evidence in favour of the contrary hypothesis, namely that the representation is in terms of concentric zones converging on the nose and mouth, must next be considered. This hypothesis, associated with the names of von Sölder, Schlesinger, Dejerine and Woods, has been formulated almost, if not quite, exclusively on observations in cases of syringobulbia. If not a few instances the cases cited as proving the correctness of this theory have lacked post-mortem confirmation. Von Sölder's paper was based entirely on clinical observation. Schlesinger in his great series of cases obtained post-mortem verification in many but too often the notes on the state of sensibility in the face were scanty or altogether absent. The reasons for adopting a critical attitude to Woods's conclusions have already been sufficiently stressed. It is not for one moment suggested that a distribution of sensory loss, such as formed the basis for this hypothesis, does not occur in syringobulbia. On the other hand by no means all cases of syringobulbia show trigeminal analgesia of concentric distribution and in this respect the conclusions of Jonesco-Sisesti, in his extensive series of cases, were contrary to the observations of earlier writers. The cases reported by Wyllie (1923) and by Taylor, Greenfield and Martin, all tend to show that the representation of the spinal tract is in terms of the peri-

pheral divisions. Taylor, Greenfield and Martin's second patient was interesting because there developed, towards the end of her life, partial analgesia and slight tactile anæsthesia in the territory of the ophthalmic nerve in the previously unaffected side. The finding of even the slightest degree of tactile anæsthesia in a case of disease limited to the medulla oblongata will require explanation later. At present it is important to consider the possible cause of the analgesia on the side which had so long remained unaffected. Fortunately the slides of this case were available for further study. In the medulla oblongata there was a typical cavity in the dorsal part of the formatio reticularis. The cavity destroyed the spinal tract and nucleus of the left trigeminal nerve but its upper limit could not be precisely determined for the brain stem had not been sectioned in its entirety. Examination at the levels of the first cervical segment and caudal part of the decussation of the pyramids disclosed that the cavity had invaded and destroyed the spinal tract and substantia gelatinosa on both sides. The cavity had, in fact, destroyed the most caudal part of the spinal tract and nucleus of the left trigeminal nerve and it is clear that this lesion was responsible for the analgesia in the territory of the left ophthalmic nerve. Were the hypothesis of Von Sölder and Schlesinger true the patient would have presented a zone of analgesia anterior to the vertex-ear-chin line. And the fact that she did not is further evidence that the notion of a segmental representation in terms of concentric zones cannot be sustained.

The hypothesis that the peripheral divisions of the trigeminal nerve are represented in an inverse order in the spinal tract and nucleus is the only theory that is in harmony with the observations here recorded. Furthermore it is in harmony with experimental observations; with clinical observations in succinct vascular lesions and with the results of comparative anatomical studies.

The position of the quintothalamic tract within the medulla oblongata and pons.—The uncertainty existing on this subject has been sufficiently indicated in the historical survey. In Case 2, it will be remembered, there was a vascular softening, limited to the retro-olivary region of one side, and so placed that it had destroyed completely the spinal tract and nucleus of the trigeminal nerve between the levels of the most caudal plane of the sensory decussation and the most cephalad fila of the glossopharyngeus. The patient lived for some two weeks and the Marchi technique was successfully applied.

A consideration of the clinical and pathological observations in this case makes it hard to escape the conclusion that the quintothalamic tract,

or, at any rate, that portion of it which originates in the cephalad three-quarters of the nucleus of the spinal tract, pursues its central course in company with the fibres of the opposite medial lemniscus. In this instance at least there is nothing in favour of the existence of a dorsal quintothalamic tract; nothing to suggest that the quintothalamic tract and spinothalamic tract are closely related in position, and only meagre evidence in favour of the existence of a short reflex central tract. It may fairly be objected that, since the lesion did not implicate the nucleus of the spinal tract at its caudal extremity, we are left in ignorance of the position of the quintothalamic pathway originating at this caudal level. This objection receives added force from the fact that the caudal extremity of the nucleus of the spinal tract is presumably related to the fibres of the ophthalmic nerve. Several factors, however, mitigate the force of this objection. In the first place the lesion implicated the nucleus of the spinal tract as low as the caudal planes of the sensory decussation. It is probable that some at any rate of the ophthalmic fibres end as far cephalad as this. Secondly it must be remembered that Cajal, Wallenberg and van Gehuchten all described fibres which passed to the ventral region of the opposite medial lemniscus when experimental lesions were situated in the most caudal levels of the medulla oblongata and, further, that they failed to find any tract of a dorsal quintothalamic tract at these caudal levels. Indeed, Wallenberg, who denied the existence of a ventral quintothalamic tract, was unable to find any trace of secondary ascending degeneration, other than in the opposite medial lemniscus, provided the lesion did not implicate the nucleus of the spinal tract cephalad to the opening of the central canal.

The hypothesis that a crossed ventral quintothalamic tract, within the system of the medial lemniscus, is the most important if not the only long central bulbar trigeminal tract is completely in accord with the clinical observations here recorded. In Case 2 sensibility on the left trigeminal field (the side contralateral to the lesion) was normal. From the crossed analgesia on the trunk and limbs it was quite certain that there was interruption of the right spinothalamic tract and examination of the medulla oblongata showed conclusively that the right retro-olivary region was extensively softened. The integrity of sensation on the left half of the face is easily comprehensible if it is assumed that the quintothalamic tract lies in the medial lemniscus, but it cannot be satisfactorily explained if it is assumed that the quintothalamic and spinothalamic are in close anatomical relation. The observations recorded in Case 1 give, by comparison, much less help. So far as they go they

confirm the view that the bulbar portion of the quintothalamic tract passes cephalad in company with the fibres of the medial lemniscus. In this case it was noted that there was a total absence of the left medial lemniscus caudal to the cephalad extremity of the cavity. Cephalad to the cavity there was a progressive increase in the number of fibres in the left medial lemniscus. At first this increase could properly be attributed to an accession of fibres from the cephalad parts of the nuclei of the posterior white columns but cephalad to the termination of these nuclei it was clear that the bulk of the left medial lemniscus was increasing. It is difficult to assign a cause for this progressive increase unless one supposes that the fibres originate in the cephalad half of the nucleus of the spinal tract of the trigeminal nerve. As the fibres in the left medial lemniscus increased it was interesting to observe that they tended to take up a ventromedial position. A comparison of Sections 32 and 44 (figs. 6 and 7) shows clearly the difference in the left medial lemniscus caudal and cephalad to the cephalad extremity of the cavity. As the sections are traced cephalad through the pons the fibres in the left medial lemniscus undergo a further change. In caudal levels of the pons the fibres maintain a medial position within the region of the medial lemniscus but, just caudal to the main sensory nucleus of the trigeminal nerve, it is apparent that the fibres in the left medial lemniscus are becoming more scattered and, in general, they occupy a more lateral position. Cephalad to the level of the main sensory nucleus of the trigeminal nerve these fibres can no longer be distinctly identified and the appearances suggest strongly that they have merged with the fibres of the spinothalamic tract. If this interpretation is correct it follows that the quintothalamic tract in man follows a course very similar to that in the rabbit, for Winkler expressly stated that the ventral quintothalamic tract of the rabbit blended with the spinothalamic tract in the cephalad half of the pons.

A critical consideration of this hypothesis of the course of the quintothalamic tract shows that its adoption does no violence to those general principles which appear to govern the disposition of the great afferent tracts within the spinal cord and brain stem. On this hypothesis the fibres mediating painful and thermal impulses from the nucleus of the spinal tract of the trigeminal nerve use the course of the opposite medial lemniscus in order to attain the cephalad part of the pons. Ultimately, it would seem, they blend with the fibres of the spinothalamic tract and thereby all impulses underlying pain and thermal sensibility from one half of the body become grouped in one tract.

At this point it becomes necessary to make a detailed examination of

certain clinical observations which, superficially, appear to negative the hypothesis that the quintothalamic tract and medial lemniscus are in close anatomical association.

Stopford (1916) has shown that the substantia alba is never nourished by the posterior inferior cerebellar artery and this observation is in full accord with the clinical findings in those cases of occlusion of the posterior inferior cerebellar artery where the trigeminal sensory loss is unilateral. A minority of the reported cases of this syndrome has, however, shown some degree of analgesia in the contralateral trigeminal territory and this demands explanation. In the instances of occlusion of the posterior inferior cerebellar artery reported up to 1937 contralateral trigeminal sensory loss was present in ten out of a total of forty-one cases. Included in these ten cases were five in which some degree of bilateral trigeminal sensory loss was present. The earlier workers were familiar with this occasional contralateral trigeminal sensory loss and Spiller (1908) referred it to implication of the quintothalamic tract. This was at a time when Spiller accepted (rather unwillingly) Wallenberg's dorsal tract as the principal quintothalamic tract. In a later publication Spiller (1915) abandoned his earlier view and adopted Dejerine's suggestion that the quintothalamic tract joined the spinothalamic tract in the retro-olivary region. This theory was also adopted by Head and Holmes (1912), by Stopford (1924, 1930), and in fact, by most English writers. In support of the localization of the quintothalamic tract in the retro-olivary region it has been suggested that the frequently observed cervical sparing implies a lamination of the spinothalamic tract and that the fibres from the cervical region probably take up a medial position in the tract. By extension it might be assumed that the fibres from the nucleus of the spinal tract of the trigeminal nerve would occupy a more medial position than those from the cervical region. However, this hypothesis, though at first sight attractive, was never fully satisfactory. In the great majority of cases of occlusion of the posterior inferior cerebellar artery coming to post-mortem examination the softening in the retro-olivary region was extensive (as in Case 2) and it is difficult to believe that any part of the spinothalamic tract could have escaped destruction. It has, indeed, been suggested that more thorough physical examination might have disclosed some degree of contralateral analgesia in many of the cases where in fact only ipsilateral trigeminal sensory loss was reported. Against this suggestion is the fact that most of the cases were reported by neurologists well aware of the possibility of the existence of contralateral trigeminal sensory defects. The resolution of this dilemma is admittedly difficult. It would be solved,

however, if it could be shown with a reasonable degree of probability that contralateral trigeminal sensory loss does not in fact occur in true examples of occlusion of the posterior inferior cerebellar artery, but only in cases in which the softening implicates the caudal levels of the pontine tegmentum. That this may be the true explanation is by no means so improbable as might appear at first sight. The following considerations will be advanced in its support. It is now well known that it may be impossible to distinguish clinically between the syndromes of the posterior inferior cerebellar and vertebral arteries and, recently, Foix, Hillemand and Schalit (1925) and Foix and Hillemand (1925) have drawn attention to a further difficulty in the way of correct anatomical diagnosis. They believe that the importance of the posterior inferior cerebellar artery in the production of the retro-olivary syndrome has been exaggerated and that other arteries may be and often are responsible. Their opinion was based on a case clinically resembling occlusion of the posterior inferior cerebellar artery but which autopsy proved to be due to occlusion of a previously unnamed branch of the basilar artery. This vessel, termed by them "*l'artère de la fosette laterale du bulbe*," is one of a pair of short circumferential arteries which arises close to the origin of the basilar artery and passes laterally to supply the retro-olivary region in the most cephalad levels of the medulla oblongata and the ventral part of the pontine tegmentum. They defined the territory of this artery by injecting the vessel in the cadaver. Foix and his fellow workers believed that many alleged examples of occlusion of the posterior inferior cerebellar artery were, in fact, examples of occlusion of the artery of the lateral medullary fossa. Of more immediate importance is the help this suggestion gives in explanation of contralateral trigeminal sensory loss in supposed occlusion of the posterior inferior cerebellar artery. An appeal to the nine reported examples of occlusion of the posterior inferior cerebellar artery in which there was sensory loss on the contralateral half of the face is, unfortunately, not very helpful, for in many of them the clinical and pathological details were scanty. Two of six cases reported by Merritt and Finland (1930) showed bilateral trigeminal sensory loss and in both these cases there was fairly clear evidence of a pontine lesion. This was shown by the presence of definite facial palsy, nerve deafness and frank abducens palsy. It is clear that signs such as these do not result from pure lesions of the medulla oblongata and consequently, as Stopford has proved, whatever the vessel occluded it could not have been the posterior inferior cerebellar artery. The case reported by Hall and Eaves (1934) under the title of "Posterior-Inferior Cerebellar Thrombosis with Unusual Features" is even more instructive. It concerned a man

who died some four months after suffering a stroke which was characterized by severe vertigo and transient facial palsy. Examination disclosed severe loss for touch, prick and temperature on the right half of the body (including the face to as high as the level of the eyebrow). Sensibility on the left half of the body (including the face) was entirely normal. At autopsy a focus of old-standing softening was found in the left half of the medulla oblongata. The nucleus and spinal tract of the trigeminal nerve were, at most, only slightly involved by the lesion. The lesion, however, quite definitely extended cephalad into the ventral part of the left pontine tegmentum. Now it must be remarked that though the case was reported as an instance of posterior inferior cerebellar arterial thrombosis the actual condition of individual vessels was not mentioned. It was merely stated that the branches of the vertebral arteries showed diffuse arteriosclerosis. It follows from what has been said previously that there must be some doubt in accepting this case as an example of thrombosis of the posterior inferior cerebellar artery. As a matter of fact the plates figuring the lesion showed that the affected area bears a striking resemblance to the territory of the artery of the lateral medullary fossa as defined by Foix and his fellow workers. In connection with the problem at issue the essential fact that emerges from a study of Hall and Eaves's case is that a contralateral sensory loss in the territory of the trigeminal nerve was found in association with a vascular softening which certainly affected the ventral and medial parts of the pontine tegmentum. A lesion in this situation may very likely interfere with the function of the medial lemniscus. A somewhat similar case came under the notice of the writer and is worthy of brief mention despite the absence of post-mortem verification.

A single man, aged 38, was admitted to the National Hospital, Queen Square (Dr. Gordon Holmes), on October 10, 1936. Three weeks previous to admission he was attacked by sudden numbness and tingling of the right half of the body. For the next two weeks nothing further happened and then there developed diplopia with inability to look to the left, severe left-sided deafness, paralysis of the left face, severe dysphagia and a tendency to fall to the right. On examination the essential findings were—complete paralysis of conjugate movement of the eyes to the left and nystagmus and diplopia on looking to the right, the left pupil was smaller than the right, severe left facial paralysis, paralysis of the left palate and absence of the left palatal reflex. There was a combination of hypoalgesia with overaction to painful stimuli on the whole of the right half of the body (including the face). In the same area there was moderate tactile anæsthesia and a severe loss of postural discrimination in the right arm and leg. There was a mild degree of hypotonia and ataxia in the right limbs. The right plantar response was extensor. The patient made a slow recovery and one year after the onset of his symptoms the only remaining abnormalities were weakness of the left face and slight hypoalgesia on

the whole of the right half of the body. The results of special investigations proved unhelpful but it was evident that he had sustained a vascular lesion of the caudal part of the left half of the pons.

Many similar cases have undoubtedly been reported as examples of occlusion of the posterior inferior cerebellar artery and in such there is no difficulty in comprehending the reason for contralateral sensory loss on the trunk and face. If these propositions are accepted there is nothing to invalidate the hypothesis that the fibres of the quintothalamic tract pursue their course through the medulla oblongata in company with the fibres of the medial lemniscus.

It only remains to comment on the lack of evidence in Case 2 for the existence of a dorsal quintothalamic tract. In this case the lesion attained its greatest proportion cephalad to the decussation of the pyramids and therefore, according to Wallenberg and van Gehuchten, it affected that part of the nucleus of the spinal tract of the trigeminal nerve which, in the rabbit, gives origin to the dorsal quintothalamic tract. It is fair to question whether or not their experimental lesions were sufficiently circumscribed. From the illustrations which they give it is evident that the experimental lesions damaged much more than the nucleus of the spinal tract. In particular they seem to have paid little attention to the descending vestibular root and it is possible that the fibres described by them as the dorsal quintothalamic tract were, in reality, fibres connecting the descending vestibular root with the medial longtitudinal bundle. The danger of such confusion was remarked on by Winkler and he hinted that this confusion had probably taken place.

In short the inferences drawn from a critical survey of previous experimental and pathological observations are in congruity with those deduced from the facts demonstrated in Case 2 of this report. Both indicate that in man the bulbar portion of the central trigeminal pathway is a crossed tract which, in the medulla oblongata at least, is incorporated with the fibres of the medial lemniscus. Cephalad to the mid-level of the pons it is probable that the fibres of the quintothalamic tract taking origin in the spinal nucleus come into a closer anatomical relationship with the fibres of the spinothalamic tract.

The central reflex pathway of the trigeminal nerve.—According to Cajal this tract, consisting of short neurones, both crossed and uncrossed, links up the trigeminal nerve with the motor nuclei of the brain stem. Winkler described a double connection between the spinal nucleus of the trigeminal nerve and the ipsilateral nucleus of the facial nerve, first a long caudal afferent arc through the most caudal part of the spinal tract and,

secondly, a short direct afferent arc at the most cephalad level of the medulla oblongata, but evidence that similar conditions apply in man has never been obtained. A survey of the published cases of the retro-olivary syndrome shows clearly that the corneal reflex once lost is lost for ever. In the majority of these cases there are good grounds for assuming that the syndrome was due to occlusion of the posterior inferior cerebellar artery and that the more cephalad levels of the medulla oblongata were unaffected by the lesion. From this it appears that in man the afferent arc of the corneal reflex is in the fibres of the ophthalmic nerve which pass to the most caudal part of the spinal tract. The evidence of the cases here reported enforces the correctness of this opinion. It is true that in Case 1 an extremely feeble corneal reflex was probably present. However, in syringobulbia it is difficult to be certain that every fibre has been destroyed in the immediate vicinity of the disease process and in this case it is possible that a few fibres of the ophthalmic nerve did, in fact, attain the most caudal part of the spinal tract. In Case 2 the most cephalad levels of the medulla oblongata were intact and, had a proximal reflex arc existed, there would have been no obvious explanation for the loss of the corneal reflex. Finally the complete abolition of the corneal reflex after section of the spinal tract in Case 3 and the similar findings in Sjöqvist's personal series of cases admits of only one explanation. Ever since the researches of G. and F. Hoggan (1883) on the nature of the nerve endings in the cornea it has been believed that the cornea is supplied solely with pain fibres. Their observations, taken in conjunction with the behaviour of the corneal reflex in lesions of the spinal tract of the trigeminal nerve, give further proof that the fibres of the ophthalmic nerve pass to the most caudal part of the spinal tract of the trigeminal nerve.

The Qualities of Sensation Mediated by the Spinal Tract of the Trigeminal Nerve.

(*a*) *Pain and thermal sensibility.*—Since the publication of the case of occlusion of the posterior inferior cerebellar artery by Hun (1897) it has been universally accepted that pain impulses from the face are mediated exclusively by the spinal tract of the trigeminal nerve. It has been equally accepted that thermal impulses pursue a similar course although it has often been suggested that the paths for heat and for cold are to some extent independent both of each other and of pain. A degree of differential thermanæsthesia was present in Case 1 where, it be remembered, loss for cold was greater than for heat. This partial and differential therman-

æsthesia coincided with a moderate degree of hypoalgesia. In the territory of the ophthalmic nerve there was almost total thermanæsthesia and analgesia. In this connection Case 3 was even more interesting for, in the territory of the right maxillary nerve, there was total analgesia and only a very moderate degree of thermanæsthesia. Few though these observations are it seems justifiable to conclude that thermal sensibility is represented in the spinal tract exactly as is pain, that is in terms of the peripheral divisions and in an inverse order. Further, the slight thermanæsthesia and total analgesia in the maxillary territory in Case 3 would be explicable on the assumption that thermal sensibility is mediated by a portion of the nucleus of the spinal tract situated rather cephalad to that concerned with the mediation of pain impulses.

(*b*) *Pressure pain.*—In regard to the possible pathways mediating pressure pain the most diverse views have been, and are, held. The apparent preservation of pressure pain following excision of the trigeminal ganglion or section of the sensory root has led many to believe that impulses underlying pressure pain travel centrally independently of the trigeminal nerve. Thus, it has been suggested by Davis (1923) that pressure pain from the face travels in the facial nerve. Others have sought a solution in the suggestion that the sympathetic nervous system may be the conductor. As a matter of fact neither clinical nor experimental evidence lends the least support to either of these views. A recent paper by Carmichael and Woollard (1933) goes far to clarify the position. They too, were puzzled by the apparent preservation of pressure pain following successful alcohol injection of the trigeminal ganglion until they discovered that the presence or absence of proper support for the subject's head and neck profoundly influenced the results. They found that if the head and neck were rigidly supported pressure pain was lost and they attributed previous contrary findings to the tension set up in the neck muscles by reason of absent or inefficient support to the head and neck. It is very regrettable that pressure pain was not estimated in Case 1 but in Case 3 it was carefully tested. It was found that after operation there was complete absence of pressure pain in the analgesia area. This was beautifully demonstrated on the right cheek by placing two fingers within the patient's mouth, thereby producing a proper counterthrust to the algometer. In this case, therefore, it seemed clear that impulses underlying pressure pain followed a course indentical with that for superficial pain.

(*c*) *Touch.*—There has been much uncertainty regarding the possible pathways for touch. No one has denied that destruction of the spinal tract

of the trigeminal nerve often leaves touch perfectly intact but this in no way proves that the main sensory nucleus is the sole receptor for tactile impulses. On the analogy of the condition in the spinal cord it has often been suggested that, in the trigeminal nerve, there exists a dual pathway for touch. From a consideration of a case of presumed disseminated sclerosis of very unusual type Spiller (1915) concluded that tactile impulses pass exclusively to the main sensory nucleus but, unfortunately, post-mortem verification was lacking.

Another problem requiring explanation concerns the frequency with which some degree of tactile anæsthesia is reported in cases where the lesion is proved to have been confined to the spinal tract. There is no need to cite specific instances. They comprise many cases of syringobulbia, for example the two reported by Taylor, Greenfield and Martin and already referred to, and many instances of occlusion of the posterior inferior cerebellar artery. A consideration of the following facts suggests that such observations may probably be fallacious. Now tactile anæsthesia is unknown in the case of lesions confined to the medulla oblongata, when loss for touch has been reported in such cases it has always been partial. The method employed in testing tactile sensibility is always of vital importance and nowhere more so than on the face. As ordinarily carried out with a wisp of cotton wool touch and tickle must almost inevitably be confused. Personal experience in patients with facial hemianalgesia has shown that they will always describe the contact of cotton wool as "less plain" or "not so strong" on the affected side. If now the sense of touch be tested with von Frey's hairs it is found that the lightest contacts are readily perceived. These facts compel a measure of scepticism in regard to the assertion that lesions of the spinal tract of the trigeminal nerve may be responsible for impaired tactile sensibility. Only careful testing with a method designed to exclude the factor of tickle will settle this question. In Cases 1 and 3 tactile sensibility was carefully estimated and it was found that on the analgesic areas the lightest contacts were felt as readily as in areas of intact sensibility. These observations do not, of course, prove that tactile impulses pass exclusively to the main sensory nucleus. On the other hand if any do travel in the spinal tract their importance must be small, so small indeed that their entire exclusion causes no appreciable rise in the threshold for touch.

(*d*) *Tactile discrimination.*—Only in Case 3 was the state of tactile discrimination investigated. Before operation the patient readily perceived two points at a separation of 0·5 to 1·0 cm. simultaneously applied in the region of the lips and cheeks and on the forehead. On re-testing the

analgesic areas after operation the state of tactile discrimination was found entirely unaffected. This observation suggests that discriminative aspects of sensibility have no important representation in the spinal tract of the trigeminal nerve. It is in keeping with the opinion that these higher discriminative functions are represented in the main sensory nucleus, an opinion which is completely in harmony with the phylogenetic history of this nucleus.

Summary.

A critical and historical review has been made of the clinical, pathological and experimental evidence bearing on the nature of the segmental representation of the spinal tract of the trigeminal nerve and on the position of the quintothalamic tract. Evidence bearing on the probable qualities of sensation mediated by the spinal tract has also been considered. On none of these problems is there general agreement; indeed opinion is more divided to-day than at any previous time. The clinical and pathological findings in three cases (syringobulbia, occlusion of the posterior inferior cerebellar artery, operative section of the spinal tract of the trigeminal nerve) are fully reported, particularly in so far as they shed light on these problems. The observations recorded are discussed in the light of previous observations.

Conclusions.

(1) In the human subject circumscribed vascular lesions are of paramount value in affording precise information on the anatomy and physiology of the brain stem. Because of the haphazard incidence of the lesion at different anatomical levels the evidence drawn from cases of syringobulbia must be closely scrutinized but, if rigid precautions are observed, valuable information may be obtained.

(2) The opinion that the representation in the spinal tract of the trigeminal nerve is in terms of concentric zones converging on the nose and mouth has been based exclusively on observations in cases of syringobulbia and, generally, in the absence of thorough post-mortem verification. No example of the retro-olivary syndrome, of vascular origin, has ever supported this opinion. In circumscribed vascular lesions of the retro-olivary region the distribution of sensory loss in the ipsilateral trigeminal territory is invariably in terms of the peripheral divisions of the trigeminal nerve.

If a lesion implicates the most caudal part of the spinal tract of the trigeminal nerve the resulting analgesia is limited to the territory of the ophthalmic nerve. If the lesion extends further cephalad (perhaps to the

level of the most caudal rootlet of the glossopharyngeal nerve) analgesia is limited to the territories of the ophthalmic and maxillary nerves. Finally, if the lesion implicates the spinal tract still more cephalad the resulting analgesia invades the whole of the trigeminal territory. These observations are incompatible with the opinion that the representation in the spinal tract is in terms of concentric zones converging on the nose and mouth. On the other hand they afford strong evidence in support of the hypothesis that the segmental representation in the spinal tract is in terms of the peripheral divisions and that the order of central representation is the inverse of the peripheral.

(3) These observations afford no evidence in favour of the existence of a dorsal quintothalamic tract; neither do they lend support to the hypothesis that the quintothalamic and spinothalamic tracts pass through the oblongata in close anatomical relationship. The observations made in one case (Case 2) justify the opinion that in the human subject the quintothalamic tract is entirely crossed and that it ascends through the medulla oblongata incorporated with the medial lemniscus. There is some evidence that the quintothalamic fibres occupy the ventromedial part of the medial lemniscus in the medulla oblongata and that finally, in the cephalad half of the pons, they come into fairly close anatomical relationship with the fibres of the spinothalamic tract. If this hypothesis be correct normal sensibility in the contralateral trigeminal territory in occlusion of the posterior inferior cerebellar artery is easily comprehended. It is suggested that the occurrence of contralateral sensory disturbance in the trigeminal area in vascular lesions results, not from occlusion of the posterior inferior cerebellar artery, but from occlusion of some other vessel.

(4) The abolition of the corneal reflex in these cases suggests that the afferent arc descends to the most caudal part of the spinal tract. If a shorter and more cephalad afferent arc exists in man it appears to be insufficient of itself to maintain the integrity of the reflex.

(5) Pain and thermal sensibility are mediated exclusively by the spinal tract of the trigeminal nerve. There is some evidence that the part of the nucleus of the spinal tract concerned with the mediation of thermal stimuli lies somewhat cephalad to the part concerned with the mediation of pain.

(6) Superficial and deep pain pursue an identical pathway in the spinal tract. There is no necessity to suppose that the facial nerve or the cervical sympathetic nerves play any part in the conduction of impulses underlying pain sensibility.

(7) The recognition of touch and the discrimination of two points simultaneously applied are independent of the spinal tract. Impulses

underlying these discriminative aspects of sensibility are, in all probability, mediated exclusively by the main sensory nucleus.

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A CHEMICAL STUDY ON FLUIDS OBTAINED FROM CEREBRAL CYSTS: REPORT ON FIFTY-SIX CASES.[1]

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CEREBRAL cysts occur with considerable frequency; according to statistics by Martin (1923) from Cushing's clinic, cystic gliomas represent 30 per cent. of all gliomas and 13 per cent. of all cerebral tumours. In spite of this, little work has been done on the fluid contents of cysts from a chemical point of view. Folin, whose results are reported in the same paper, examined the cyst fluids of seven cases of gliomatous cysts. His estimation of various fractions of non-protein nitrogen gave the following average results:—

N of amino acids	5·3 mg. per 100 c.c.
N of urea	12·4 mg. per 100 c.c.
N undetermined	6·7 mg. per 100 c.c.
Total N (non-protein)	24·7 mg. per 100 c.c.

If the cyst fluid were produced by breakdown of tissue only, one would expect much higher readings of amino acids. Therefore Martin explained the results as due to transudation from the blood. The following investigation was undertaken: (1) To obtain average results of various constituents of cerebral cysts; (2) to estimate their diagnostic value; and (3) to contribute to the theory of cyst formation.

METHODS AND MATERIAL.

In fifty-six cases the cyst fluid was examined chemically. The fluid was usually obtained at operation, but in a few cases it was obtained at post mortem. The specimens were cleared by centrifuging. Whenever it was possible, duplicate estimations were undertaken. In a number of cases parallel estimations of the blood were carried out. The blood was obtained from veins of the arm or leg, usually a few hours after the operation, or in a few cases during the operation—that is to say, almost simultaneously with the withdrawal of cyst fluid. The number of chemical constituents examined depended on the amount of available material.

[1] This investigation was carried out while holding the Kathleen Schlesinger Fellowship.

Substance	Number of estimations	Parallel estimations in the blood	Parallel estimations in the ventricular fluid
Albumin and Globulin	21	11	—
Cl.	45	15	3
Ca.	25	5	3
Mg.	26	7	4
Glucose	7	—	1
Urea	12	8	1

For albumin and globulin the method of Greenberg (1929) was applied. Calcium was estimated according to Kramer and Tisdall (Harrison, 1937), magnesium and chlorides according to McCance and Shipp (1933), glucose according to Folin and Wu, and urea according to Archer's modification of Folin and Wu's method (Harrison, 1937).

Results.

The results are given in detail in the accompanying tables. It can be seen that the protein content of the cyst is always lower than that of the blood. The globulin in the cyst fluid is usually low, so that the albumin/globulin ratio amounts to an average value of 3·7, compared with the average ratio in the blood protein readings of 2·8. This is particularly remarkable in two tumours of mesodermal origin (Co. 21.4.36 and Hu. 7.5.37), in which the albumin reading in the blood and cyst is identical, and the globulin content of the cyst is lower. During puncture or incision of the cyst a mixture of the cyst fluid with cerebrospinal fluid cannot be avoided in every case; this accounts for the comparatively low protein reading in case "Mi. 8.6.38," and it may account for a few other exceptionally low protein readings. The amount of chloride is constantly higher in the cyst fluid than in the blood, with the exception of one case in which the histological diagnosis was that of a cystic condition of the choroid plexus of unknown nature. The calcium content is either that of the blood calcium or lower, between 6·6 and 10·4 mg. per cent. In the case of a cystic oligodendroglioma, however, it amounted to 11·4 mg. per cent. Magnesium, with the exception of one low reading (1·23 mg. per-cent.), ranges between 2·18 and 4·1 mg. per cent., that is to say, it corresponds with the normal magnesium content of the blood. The differences between blood and cyst fluid in the individual cases, however, are irregular. Urea shows a similar behaviour to calcium. It corresponds with the blood urea or is somewhat lower (two cases). For technical reasons, simultaneous parallel estimations of glucose in the blood could not be made; the amounts of glucose in the cysts, however, are either readings corresponding to the blood sugar of average individuals, or somewhat below it.

TABLE I.

Name and date	Material	Alb. g. %	Glob. g. %	Chlorides as NaCl. mg. %	Ca. mg. %	Mg. mg. %	Diagnosis and Notes
Sm. 3.6.38	Cyst Blood	1·33 4·1	0·40 2·99				Parieto-temporal cyst, histology unknown
J. G. 7.6.38	Cyst Blood	3·98 5·84	1·61 3·98	571 543			Cancer of lung, secondary in R. hem., cystic
Wo. 16.6.38	Cyst Blood	1·46 4·51	0·69 1·72				Cerebellar cyst
Wo. 21.6.38	Cyst Blood	2·66 5·48	0·75 1·6	643 590			Cerebellar cyst
Yo. 16.7.38	Cyst	3·98	1·73	578			Parieto-temporal cyst (? glioma)
Yo. 21.7.38	Cyst Blood	3·98 5·57	1·38 1·5	580 557			
M. C. 21.4.36	Cyst Blood	4·78 4·78	0·92 1·84				Cystic neurofibroma, R. ponto-cerebellar angle
C. J. 22.9.36	Cyst Blood	6·9 7·24	0·92 2·30	796	10·0 10·4	5·91 4·18	Cystic glioma, parietal
Ha. 14.10.38	Cyst Blood	3·79 4·30	1·29 1·61				Subdural hæmatoma
Ad. 21.4.36	Cyst Blood	1·33 4·20	0·23 1·1				Polar spongioblastoma
Pe. 14.7.36	Cyst Blood	3·45 4·94	1·15 1·44				Suprasellar cranio-buccal cyst, simple epitheloid
Hu. 7.5.37	Cyst Blood	3·19 3·19	0·82 1·61	585 410	9·4 9·8	2·58 2·53	Recurrent cerebellar cyst. Hæmangioblastoma
Mi. 8.6.38	Cyst	1·06	0·40	655			Glioma of basal ganglia. Cyst fluid obtained p.m., mixed with c.s.f.
E. J. 30.6.38	Cyst	3·98	0·80	524			Parietal cyst (histology unknown)
Co. 5.7.38	Cyst	2·92	1·72	623			Chromophobe adenoma of pituitary. Cyst fluid obtained p.m.
Fr. 15.7.38	Cyst	4·25	0·75	730			Cystadenoma of infundibulum Cyst fluid obtained p.m.
Me. 21.7.38		2·17	0·35	676			Left parietal cyst
Pu. 28.9.38	Cyst	4·25	1·1				Parietal astrocytoma
Pe. 7.10.38	Cyst	4·14	1·05				Cyst fluid obtained p.m., very blood-stained, hæmolysis
Ma. 10.10.38	Cyst	3·50	1·34				Epithelial tumour of Rathke's pouch. Cyst fl. obtained p.m.
Ch. 6.10.36	Cyst	6·39	1·3				Cerebellar astrocytoma

TABLE II.

Name and date	Material	Ca. mg. %	Mg. mg. %	NaCl mg. %	Glucose mg. %	Urea mg. %	Diagnosis and Notes
Ad. 21.4.36	Cyst Blood	6·6 10·4	1·23 3·08	646			Fronto-parietal spongioblastoma
L. J. 23.3.37	Cyst Blood Ventr. fluid			540 477 702			R. temporal astrocytoma
Al. 25.7.37	Cyst Blood			562 406		32 43	R. frontal gliomatous cyst
A. T. 11.2.38	Cyst Ventr. fluid			646 746	53 70	24 27	Cerebellar astrocytoma
C. J. 22.9.36	Cyst Blood	10·0 10·4		796			Parietal glioma
Ag. 5.6.36	Cyst Blood R. vent. fluid		3·07 2·52 3·07				Suprasellar fibrous astrocytoma
Ho. 1.10.36	Cyst Ventr. fluid	7·6 4·0	4·1 3·44	671·6			R. temporo-parietal glioblastoma
Fr. 29.8.36	Cyst Ventr. fluid	9·2 6·4	2·18 2·18				Ventricular tumour in tuberous sclerosis
Ma. 12.3.37	Cyst Blood	9·8 9·5					Parietal astrocytoma
Ba. 6.1.38	Cyst Blood			613 522	55	18 22	Simple cyst of Rathke's pouch
Co. 18.1.38	Cyst Blood			599 629	103	54 54	Cystic condition of choroid plexus
J. R. 25.11.37	Cyst Blood	10·4	2·48 2·46	617·6 603·7			R. ponto-cerebellar angle hæmangioblastoma
R. F. 2.3.37	Cyst Blood	8·0 9·0	2·78 2·21	552 559			R. parietal cyst, hæmangioblastoma (?)
St. 10.7.36	Cyst Blood		3·05 2·56				Secondary (intestinal ?) tumour of cerebellum
Wa. 4.2.38	Cyst Blood					70 72	Secondary from bronchial carcinoma
Hu.(1st op.) 7.5.37	Cyst Blood	9·4 9·8	2·58 2·32	585 410			Recurrent L. cerebellar cyst ; hæmangioblastoma
2nd op. 8.6.37	Cyst Blood		2·48 4·46	612 557			
3rd op. 5.11.37	Cyst	9·4	2·22	643			

TABLE II.—*Continued.*

Name and date	Material	Ca. mg. %	Mg. mg. %	NaCl. mg. %	Glucose mg. %	Urea mg. %	Diagnosis and Notes
Hi. 17.12.37	Cyst Blood			662 634	67	20 19	Cerebellar cyst. Nature unknown
Le. 23.12.36	Cyst Blood	10·4	2·65	590 515			Frontal cyst. Brownish fluid full of cholesterin crystals, Hist.: Fibrous tissue with some calcareous masses
Wi.(1st op.) 30.11.37	Cyst Ventr. fluid	8·0 3·4	2·97 3·58	569 744			Occipital cyst. Nature unknown
2nd op. 21.1.38	Cyst Blood			590 585		31 29	
Ap. 24.1.38	Cyst Blood			569 569		25 35	Occipital cyst of unknown origin
Hu. 4.2.38	Cyst Blood			542 514		29 26	Tumour of cauda equina
No. 25.11.36	Cyst	10·2	3·08	613			Cerebellar astrocytoma. Fluid obtained at p.m.
Cu. 5.3.37	Cyst	11·4	2·13	519			Parietal oligodendroglioma
Ha. 12.3.37	Cyst	7·2	3·05	625			Glioblastoma. R. frontal. Fluid obtained at p.m.
Pe. 2.4.37	Cyst	9·2	2·32	526			Diffuse glioblastoma. L. frontal
Ha. 8.6.37	Cyst	8·8	2·95	652			Parietal glioblastoma
Cl. 12.7.37	Cyst	7·2	2·09	601			Fronto-parietal glioblastoma
Ho. 17.9.37	Cyst	7·6	3·53	632			Cerebellar astrocytoma
Ca. 24.9.37	Cyst	9·0	3·32	648			Cerebellar astrocytoma
To. 16.11.37	Cyst	7·8		630			Thalamic astrocytoma
Pa. 7.1.38	Cyst			642			Frontal astrocytoma
Cr. 19.4.38	Cyst				77	45	Parieto-frontal astrocytoma
Lo. 24.3.38	Cyst				75	38	Suprasellar cyst, fluid containing cholesterol crystals
We. 24.6.37	Cyst		3·7	492			Acidophil adenoma of pituitary

TABLE II.—*Continued.*

Name and date	Material	Ca. mg. %	Mg. mg. %	NaCl. mg. %	Glucose mg. %	Urea mg. %	Diagnosis and Notes
Dr. 11.11.37	Cyst	9·2	2· 2	589			Adamantinoma
Ch. 23.9.37	Cyst	8·6	2·21	585			Cerebellar capillary hæmangioblastoma
Da. 22.6.37	Cyst	8·8	2·46	578			Acoustic nerve tumour
Va. 1.7.37	Cyst	10·2	3·32	552			Secondary carcinoma from lung. Temporal. Fluid obtained at p.m.
Da. 24.12.36	Cyst	9·2	2·95	768			Cerebellar cyst of unknown origin. Hist. : Normal cerebellar cortex
Li. 24.3.38	Cyst				62	24	Cerebral cyst, nature unknown. Hist. : Normal septum pellucidum

Discussion.

From the comparison of the readings of the various substances examined with the histological diagnosis, it is apparent that there is no connection between the histological nature of the cyst and the chemical composition of the fluid. The only finding which is conspicuous from this point of view is the fact that the only calcium reading which was comparatively high was that encountered in a case of oligodendroglioma. This is interesting, because of the frequency with which calcium deposits are found histologically in these tumours. Only investigations on the basis of a larger amount of material of the same sort can prove whether this single finding was a mere coincidence, or whether it has any diagnostic value. A second important point is the complete independence of the chemical composition of the cyst fluid on the site of the cyst, especially on its relation to the cerebrospinal fluid spaces.

The chlorides, with only one exception, were constantly higher in the cysts than in the blood, whereas the protein was constantly lower. How is this regularity to be explained ? It has been shown by previous investigators that in transudates from the blood (Loeb *et al.*, 1922, Gollwitzer-Meyer, 1925) this reciprocal proportion is the rule, and that it can be explained on the basis of the Donnan equilibrium. This suggests that the formation of cyst fluids is due to the same mechanism. Moreover,

the investigations of Loeb *et al.* showed that in transudates, as well as exudates, calcium, urea and glucose were approximately the same in both blood and fluid. Gollwitzer-Meyer found in transudates (renal and cardial) that the calcium content was always somewhat lower than in the blood. In the present cases of cerebral cysts the amounts of calcium, as well as urea, were either equal to those in the blood or were somewhat lower. In the latter case the calcium ratios between blood and fluid corresponded to those found by Gollwitzer-Meyer in renal and cardial transudates. All this strongly supports the assumption already made that the cyst fluid is derived essentially from the blood. The protein readings, however, are much higher than those of pure transudates as encountered in renal and cardial diseases. They are much more like those of true inflammatory exudates. Schade *et al.* (1926) found total protein quantities of 3·4 to 5·8 grm. per cent. in inflammatory pleural and peritoneal exudates. This corresponds approximately to the magnitude of total protein in cyst fluids. It can be assumed that the histologically abnormal vessels in tumours and the proliferative vascular reaction in the surrounding zone of tumours and cysts provides a state of increased permeability which accounts for those high protein readings. From all this one can draw the conclusion that following the initial colliquative necrosis of tumour tissue the essential process is that of transudation from the blood into the liquefied area ; this, of course, does not exclude the presence of products of break-down in the fluid, but of these very little evidence was found. It is interesting in this connection that the chloride ratio of blood and fluid was the typical one, even in a case of hæmangioblastoma in two examinations at four-week intervals. This supports the view that cysts in hæmangioblastomas are true cysts and do not represent a direct continuation of the intravascular space.

Munro and Merritt (1936) have shown in a study on 105 cases of subdural hæmatoma that the chemical picture of the fluid depends on the age of the cyst. During an initial period the protein increases owing to hæmolysis ; later it decreases owing to a breakdown of protein molecules. An increase of the amount of fluid occurs coincidentally because of the dialysis of fluid from the cerebrospinal fluid space. In the present paper the problem of the formation of subdural hæmatomas was not specially studied as hæmolysis and the adjoining cerebrospinal fluid space appeared to provide somewhat different conditions. It should, however, be stressed that from the survey of the present cases it appears that there is no certain relation between the age of the cyst and the protein content.

SUMMARY.

Estimations of various constituents of cyst fluids in fifty-six cases of cerebral cysts gave the following results:—

The protein content in the cyst fluid is constantly lower than that in the blood, the chloride content being always higher. The calcium content of the cyst fluid either corresponds to that of the blood or is somewhat lower; the same holds true with the urea content. The amounts of glucose correspond to average blood-sugar values, or are somewhat lower.

These findings are analogous to those obtained by previous authors in transudates from the blood other than cyst fluids. The comparatively high amounts of protein which resemble those of inflammatory exudates is explained by the high permeability of pathological vessels and by mesodermal reactive processes. There is no relation between the chemical nature of the fluid on the one hand and the site or histological nature of the cyst on the other. A comparatively high amount of calcium (11·4 mg. per cent.) was found in a cystic oligodendroglioma.

I wish to express my gratitude to Dr. J. G. Greenfield and to Dr. J. N. Cumings for help and suggestions, to Mr. R. F. Nunn, B.Sc., for technical advice, and to the members of the surgical staff for their helpful co-operation.

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SPASTIC DYSPHONIA (" INSPIRATORY SPEECH ").

BY MACDONALD CRITCHLEY.

THE purpose of this paper is to call attention to a peculiar disorder of articulation which has been treated somewhat perfunctorily in the literature. This form of speech disturbance has been encountered in a few patients, three of whom are described below. One or two publications give accounts of a dysarthria which suggest the same type of speech-disorder as concerns us here. Numerous descriptive epithets have been applied such as " seelöwen Sprache," but the commonest term has been " inspiratory speech." Various diagnoses have been proffered in these cases, especially disseminated sclerosis, double athetosis, and progressive cerebellar degeneration.

The characteristics of the speech defect may be described as follows: the voice sounds are emitted in a peculiarly harsh and constrained fashion, the pitch being at times unduly low and at others excessively high. The word-sequence is interrupted so that a staccato effect is produced. The volume of the sound seems uncontrolled and words may be spoken too loudly interrupting in an explosive fashion a sequence of subdued tones. At times there is a tremolo effect audible, suggesting a tremulous condition in the respiratory or articulatory musculature. Not only is the pronunciation of the consonantal sounds affected to a slight degree, but the vowel sounds too are modified, differing in this respect from the commoner types of dysarthria. There is an impairment of the so-called " chanson de parler " so that the speech tends towards a monotone. There is always an excessive play of facial expressive movements with the accompaniment of an associated tic-like contraction of the muscles of the neck and jaws, and even of the shoulder-girdle and upper arm. Throughout the act of speaking there appears to be a striking hypertonus in the extrinsic muscles of the larynx which waxes and wanes with the involuntary movements; in this way there results a peculiarly forced character in the speech, which appears difficult of accomplishment, almost as though the patient were trying to talk whilst being choked. Although the whole of the speech takes place during expiration, the sound-effect is unnatural and suggests the picturesque though incorrect title of " inspiratory speech."

The larynx was examined in two of the patients. In one case (No. 1)

no obvious abnormality was seen in the palatal or laryngeal muscles, except that the ventricular bands did not come into apposition ; there was no evidence of involuntary motor activity. The other patient (No. 3) displayed jerky movements of the vocal cords, analogous with a series of clonic movements of the palate and tongue associated with the act of phonation.

It is possible that this type of speech was present in the first case recorded by Ramsay Hunt (1914) of " dyssynergia cerebellaris progressiva." The author described the speech as slow, scanning and frequently interrupted by violent explosive efforts and utterances. Under excitement these rendered the speech almost unintelligible. The act of speaking was associated in this case with tremulous contraction of the face and increased tremor of the head. In the other two cases described by Ramsay Hunt, the speech affection did not resemble the type under discussion.

Most relevant, however, are the descriptions of dysarthria made by Schuster (1924) in his cases of senile cerebellar degeneration. His first patient, a woman of 71, showed an explosive, nasal, slowed, scanning speech. Labials were especially badly pronounced. In the middle of a phrase or a word, the loudness of the voice might suddenly increase or decrease. The speech was mainly monotonous and there were frequent false intonations. It was difficult to understand what she said. There was a tremor of the head which increased as she spoke. In his second case, a woman of 63, the speech was described as slow and scanning, with interruptions in the middle of a word. Clonic movements of the head often synchronized with a jerkiness of the speech. The third patient, a woman of 58, spoke slowly with a loud explosive, nasal dysarthria, as though someone were clutching her by the throat while she was trying to speak. Schuster also referred to a similar dysarthria occurring in two patients with cerebellar vascular lesions, and in a third patient who showed a delayed form of heredo-familial cerebellar ataxia. The author emphasized that the dysarthria differed from the usual scanning speech of cerebellar disease . . . " Die Sprache unserer Kleinhirnkranken errinerte zwar die gewöhnlich als 'skandierende' Sprache bezeichnete ; denn sie war gleichfalls sehr verlangsamt, gedehnt und schwerfälling, sie hatte aber ausserdem noch eine besondere Note, welche keiner der bekannten anderen Sprachstörungen zukommt, und welche sich schwer beschreiben lässt. Sie klang ungefähr so, als wenn jemand, denn man die Gurgel zuhält, mit aller Kraft und Anstrengung zu sprechen versucht, sie war überlaut und in ihrer Klangfarbe gänzlich won den normalen verschieden. Häufig kamen dabei inspiratorische, leicht schluchzende Töne vor, die man normalerweise überhaupt nicht aus dem

menschlichen Kehlkopf vernimmt, sondern wie man sie etwa bei dem eigentümlichen Bellen der Seelöwen hört. (Diesen eigentümlichen 'Seelöwenton' habe ich nur noch einige Male bei Patienten mit Athetose double vernommen.)"

It may be that this same variety of speech was familiar to Meige. This author, who has devoted much attention to disorders of speech, has analysed closely the processes at fault (1928). He distinguishes faulty habits of pronunciation from various disorders of elocution. Of the latter, he recognizes (1) an atonic or inhibitory type; (2) a tetaniform or tonic convulsive variety (= stammering); and (3) a palisyllabic or clonic convulsive type (=stuttering). Concomitant motor symptoms, such as tic-like grimacing may occur in each. With regard to the vocal manifestations of the elocutionary disorders, defects can be traced in the mechanisms of respiration (dyspneumia), phonation (dysphonia) and articulation (dysarthria). Meige points out that the ætiology is complex and that all these may be encountered in a number of organic affections of the nervous system. A case record of his own (1914) entitled "Dysphasie singultueuse avec réactions motrices tetaniformes et gestes stéréotypes" deals with a speech affection in a girl of 13 which seems to resemble that occurring in the third of the patients here described.

Personal Cases.

No. 1.—L. L. J., male, aged 28, was admitted to King's College Hospital from September 1 to November 29, 1937.

In 1932 whilst in the Royal Navy, he accidentally sucked up some petrol from a pipe, so that the naval surgeon had to wash out his stomach. Thereafter he noticed a tremor in the left hand. Examination at that time revealed exaggerated knee and ankle jerks and intention tremor of the left upper limb. There was some doubtful pallor of the outer halves of the optic discs. The blood and spinal fluid were normal. He was discharged from the Navy the same year as a suspected case of disseminated sclerosis.

Eighteen months later he enlisted in the Army. One day, however, he found while on parade that he was unable to keep his head turned to the front . . . "When we had to present arms everyone faced the front but me." As a result he was re-examined and invalided out of the Army in July, 1934. By this time, the tremor had increased in the left arm and two months later the involuntary turning movements of the head became worse. At this time he first began to have trouble with his speech.

Family history.—His father had died of phthisis; the mother was said to "fall about." There were two brothers and one sister, as well as three step-brothers and one step-sister, all of whom were described as normal.

Examination.—The patient showed a spasmodic torticollis, with jerkings of the chin upwards and to the left, and with myoclonic movements of small range in the muscles around the right corner of the mouth. The outstretched hand displayed

on the left side a rhythmic tremor, considerably increased on voluntary movement. None of the arm-jerks was obtainable except the left triceps reflex. There was no defect of tonus or of motor power in the legs. The knee-jerks were present but the ankle-jerks absent; plantar responses were flexor. Abdominal reflexes intact. The temporal portions of the optic discs were possibly a little too pale. All forms of sensation were somewhat impaired over the left half of the body.

The *speech* was hoarse and jerky, the sounds being breathless and constrained. The vowels were pronounced imperfectly. Towards the end of a sentence the voice tended to become less audible.

X-ray screening of the chest revealed that the movements of the diaphragm during respiration and speech were normal with no evidence of tremor.

Examination of the pharynx and larynx (Mr. Victor Negus): " No abnormal movements of the palate, which moves well and apparently quickly. Palato-glossus and palato-pharyngeus contract well on both sides. Posterior pharyngeal wall rises well on phonation. Larynx moves upwards on ' ee ' and remains in mid-line. Vocal cords move well and equally on phonation. Larynx opens widely on normal respiration. No nystagmus of larynx. I do not think he speaks during inspiration . . . I think the disorder of speech is due to inco-ordination of respiration and articulation."

Cerebrospinal fluid.—Initial pressure 120, rising to 300 on jugular compression. Less than two cells per cubic millimetre; protein 40; chlorides 720. Wassermann negative.

The patient was regarded as having a striato-cerebellar affection with symptomatic torticollis. Disseminated sclerosis was regarded as improbable.

No. 2.—J. S., male, aged 42, first attended the out-patient department of the National Hospital, Queen Square, in November, 1921. He was admitted under the care of Dr. Kinnier Wilson between April 13 and July 14, 1933, with the diagnosis of disseminated sclerosis.

Weakness of the legs had developed gradually since 1918, and since 1923 there had been unsteadiness in walking. The arms became weak and clumsy in 1928, and since 1927 there had been at times urinary and less often rectal incontinence. Difficulty in speaking first became apparent in 1921.

The family history was negative in respect of nervous disease.

Examination.—There were a few irregular nystagmoid movements on full lateral deviation of the eyes. Both legs were spastic and somewhat weak. The lower abdominal reflexes were sluggish; knee and ankle jerks exaggerated; both plantar responses extensor. Except for some diminution of postural sensibility in the lower limbs, sensation was normal.

Cerebrospinal fluid.—One cell per cubic millimetre; protein 75; Nonne-Apelt negative; Pandy weakly positive; Lange, no change; Wassermann negative in fluid and in blood.

The speech was described in 1921 as " strained, high-pitched, slightly staccato—as though speaking in inspiration."

According to the notes made in 1933, the speech was " guttural, low-pitched, spastic and unvarying . . . no evident dyspnœa at rest or in talking."

No. 3.—E. G., male, aged 40, was a patient at the National Hospital, Queen Square, under the care of Dr. W. Aldren Turner from May 5 to July 16, 1925. Three years

before he had been an in-patient of King's College Hospital (Dr. Tunnicliffe) for the same disorder.

At the age of 15, some fireworks had been surreptitiously attached to his coat-tails and then lighted. The resulting fright was intense and trouble with articulation dated from that incident. Previously he had won prizes at school for elocution. Weakness and spasm in the arms and hands first appeared in 1914, that is at the age of 29. Twitching of the face first developed in 1921.

According to his wife, the patient's speech was abnormal when she first knew him, i.e. twenty-two years before, but the hands were not affected until about four years ago.

Family history.—Eleven children ; one was said to stutter and to have deformed feet ; another showed excessive sleepiness.

Mother died from a stroke ; the father, aged 69, suffered from a similar though slighter affection of the speech ; there was no trouble with his arms (the wife stated that her father-in-law's speech was gruffer than her husband's and that he did not contort his face as he spoke ; neither did he stammer).

It is believed that the paternal grandmother had a tremor of the hands and an affection of the speech.

One brother and one sister were alive and quite healthy.

Examination.—Very fine lateral tremor of the mandible ; slight relative weakness of the left side of the face. The head was held tilted slightly over to the right, but there were no clonic involuntary movements. Coarse fibrillary tremors were present in the tongue. When the patient phonated, the tongue shot in and out and the palate rose and fell in a series of parakinetic movements.

Both hands were held with the fingers flexed into the palms. Tonus was increased in the distal parts of the upper limbs. Under emotional stress and on voluntary movement both hands showed a coarse, irregular, undulating tremor of the fingers, more evident on the right side. Voluntary power was good except for an inability to extend the fingers. All digital movements were awkward, inco-ordinate and slow.

Sensory testing revealed no abnormality. All the tendon-jerks were present and equal ; abdominal responses elicited ; plantar reflexes flexor.

Cerebrospinal fluid.—Five cells per cubic millimetre. Protein 40. Lange 0001110000. Wassermann negative in fluid and blood.

Larynx (Mr. Theodore Just).—" Abduction and adduction of cords full ; the movements are jerky and are similar to the movements of the tongue and palate."

Speech.—The articulation was grossly defective and inco-ordinate so that it was only with the utmost difficulty that one could understand him. When he attempted to speak he would tilt his head to the right and screw up the left eye. The face would then show a series of extraordinary grimaces and the complexion become flushed. " Speech is pre-eminently inspiratory in type, is grossly inco-ordinate and breathless. Occasionally he stammers over a syllable. Labials and dentals are uttered in an explosive fashion. There is a tendency for the syllables to be separated in a staccato fashion. During the effort of speaking the right arm shows a series of involuntary movements."

The diagnosis of double athetosis was hazarded. (In King's College Hospital the condition was regarded as probably an hysterical affection.)

Discussion.

In the three cases here described a clinical diagnosis cannot be arrived at with certitude. The first two patients were regarded, at one time at least, as suffering from disseminated sclerosis. This is probably not the correct explanation of the symptoms in the first case and the diagnosis is not unassailable in the second. The third patient was never diagnosed with any degree of confidence and it is open to argument whether indeed any organic neurological affection existed.

Similar speech disorder has been described by Schuster in cases of senile cerebellar degeneration; cerebellar vascular disease; delayed cerebellar ataxia; and double athetosis. One of Ramsay Hunt's cases of so-called dyssynergia cerebellaris progressiva may be quoted in this connection. Some of the more complex cases of stammering and stuttering recorded by Meige suggest a somewhat similar type of speech.

In most of the cases there were evidences of cerebellar dysfunction. The presence of hypertonus and involuntary movements complicates the picture, however, and suggests that pyramidal lesions may be coexistent in some cases, and extrapyramidal motor disease in others. Although inco-ordinate respiration is demonstrable in the speech of most patients with cerebellar and with striatal affections, the speech disorder which concerns us here differs considerably from what is commonly encountered.

Terminology presents various difficulties, for it is not easy to suggest a word or phrase which clearly expresses the peculiarities of this speech disorder. " Inspiratory speech " had the merit of drawing attention to an unusual type of dysarthria and of attempting to describe its clinical peculiarities; unfortunately its use is unjustifiable as it is essentially inaccurate. Even the term " dysarthria " can be criticized as the articulation of consonants is less severely disordered than the pronunciation of vowels. The trouble concerns phonation as least as much as articulation. Because of the peculiar strained or forced character of the voice, suggesting a spasmodic action of the intrinsic and extrinsic laryngeal musculature, the term " spastic dysphonia " is perhaps least open to objection. The alternative terms " dystonic dysphonia " or " dystonia-dysarthria " are perhaps too cumbersome.

The general question of respiration in normal and disordered speech merits some attention. Under physiological conditions, the act of speaking both in quiet conversation and in declaiming, takes place entirely during the expiratory phase of breathing. The lungs refill by means of a deep inspiration quickly and unconsciously made during pauses in the oration.

In singing this becomes a matter of some difficulty, and may cease to be a purely automatic activity. Training ensures a correct co-ordination between the acts of respiration and of voice production. Indeed, only in whispered speech is it possible to speak upon an inspiratory phase.

In various pathological states, and especially in cerebellar syndromes, there is a considerable disturbance not only in the harmonious working of the numerous articulatory muscles but also in their co-ordination with the respiratory musculature. The resulting dysarthria therefore betrays frequent faults in breathing; the voice is emitted either too loudly or too softly, and the patient soon becomes breathless. At no time, however, does the patient consistently articulate during the phase of inspiration.

Nevertheless, inspiratory sounds may participate in the cries and utterances of various animals, e.g. donkeys and horses, due, as Negus (1929) has pointed out, to the feeble valvular nature of their larynx. The purring of some of the cat tribe takes place during both inspiration and expiration. A bird, of course, can easily produce sounds during both phases of respiration, because of the anatomical nature of the syrinx and its connection with capacious air sacs. In addition various sounds and interjections of an inspiratory character may find their way into human speech as occasional utterances, thus constituting fragmentary exceptions to the rule.

The best instance of the persistent occurrence of inspiratory sounds in articulate speech is encountered in the Hottentot group of languages. The "cerebral," dental, labial, and palatal "clicks" typical of that philological group are mainly inspiratory sounds and in normal speech they interrupt the ordinary stream of expiratory utterance.

In the near East, and especially Turkey, a palatal clicking sound, made on inspiration, is commonly used in association with a backward jerking movement of the head to denote negation. This can be regarded less as a form of speech than an audible gesture.

Hissing inspiratory sounds made by an indrawing of the breath between the closed teeth, may constitute a type of "inferior speech" in the sense of Hughlings Jackson. They are well known in Japan as an audible "honorific" expression denoting respect. The same hissing noise is sometimes used as an interjection signifying assent and is common in this connection in Devonshire. According to Cranz (1873) Greenlanders also have a sound to express pleasurable affirmation, made by sucking air down their throats. Some other primitive languages, as in Tierra del Fuego and in parts of North West America, include strange clucking, grunting and gurgling noises, some of which are inspiratory.

SUMMARY.

Attention is directed to an uncommon and peculiar type of speech-affection, whereby the voice is emitted in a constrained, forced, and barely intelligible fashion. There is also an imperfect modulation of the voice together with a faulty pronunciation of vowel and consonantal sounds. Frequently tic-like contractions of the face, neck, and even upper limbs may accompany the act of speaking.

A few records have been found in the literature describing this type of speech in association with various disorders, e.g. progressive cerebellar degeneration, and double athetosis. Three personal cases are here described wherein this type of speech occurred; no confident diagnosis could be made in these cases.

The term "spastic dysphonia" is suggested as a clinical descriptive epithet. In the past, the expression "inspiratory speech" has been used, but incorrectly, for the whole of the speech takes place during the phase of expiration, as ordinarily.

Short mention is made of the exceptional instances of inspiratory sounds in human and animal speech.

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THE CLINICAL RECOGNITION OF PICK'S DISEASE: REPORT OF THREE CASES.

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DURING the past few years there has been an increasing number of publications dealing with that variety of heredopathic involution described by Pick. New facts have been brought to light by research along anatomical as well as genetic lines. The recognition of clinical sub-types, and the more thorough clinical descriptions of the disease have rendered diagnosis of the cases easier. Nevertheless, in early cases where symptoms are few, diagnosis may present serious difficulties. In such cases it may be necessary to resort, not only to Neisser-Pollack's brain puncture, but also to angio- and encephalography. We are recording in this paper three cases of Pick's disease diagnosed during life, each presenting peculiar arteriographic and ventriculo-encephalographic features.

CASE REPORT.

Case 1.—S. S., female, aged 57, was under observation in the University Neurological and Mental Hospital, Budapest, from May to June 7, 1938. *Family history:* Her father had two apoplectic fits with subsequent "insanity" and died at the age of 37. Her mother is said to have suffered from melancholia and died in hospital at the age of 60. A sister of her mother died "insane" at 70; a brother committed suicide at 50. *Personal history:* Climacteric five years before admission. During the last year the patient had become exceedingly absent-minded, being unable to do her housework, to cook or to take charge of money. During the week preceding her admission she showed some mental excitement. *Neurological examination:* The pupils were of average size, equal and regular, reacting normally to light and on accommodation. The other cranial nerves were normal. There were senile changes in the fundus. All tendon, periosteal and skin reflexes were normal. There were no pathological reflexes and no trace of clonus. The naso-oral and naso-mental reflexes were well-marked. Grasping and groping phenomena were present on both sides, more especially the right. Apart from these signs there were no motor or sensory disturbances.

The area of cardiac dullness and the heart sounds were normal; the pulse regular, the blood-pressure 115/75 mm. *Laboratory examinations:* Urine normal; Wassermann test in blood and cerebrospinal fluid negative. Cell count in the cerebrospinal 0, total albumin 17 mgm. per cent., the globulin reactions as well as the various colloidal reactions normal. *Mental findings*: *Speech*: was normal except for slight

articulatory uncertainty with difficult test-phrases; there was, however, no definite dysarthria. Reading, writing, copying and drawing showed no noteworthy defect. There was no evidence of aphasia, apraxia or agnosia. She was uncritical, apathetic and devoid of initiative, remaining inactive throughout the day or else following passively the example of her fellow patients. She could comprehend simple commands, but complicated orders presented serious difficulties. Her attention was much impaired; she failed entirely in Bourdon's test, and showed a marked inability to attend to stimuli. *Memory:* while she had retained engrams of older date, she

FIG. 1.

was incapable of remembering a date or a name given her a few seconds before, if her attention had been diverted for a moment, even though she had been warned to concentrate on the test. She could repeat immediately twelve syllables or four digits, but was unable to remember two digits after her attention had been distracted for a second. There was no confabulation. Her consciousness was unimpaired, the autopsychic orientation as well as the orientation in space was good. She was, however, completely disoriented in time, and was unable to say whether she had been in the hospital for a day, a week, or a month, what was the season, the day or

the time of the day. Her association was slow, poor and unproductive. There were no delusions. Her intelligence showed an uneven but grave impairment. Binet-Simon tests gave an age of nine years. Emotionally she was responsive, and affectionate towards her relatives.

Encephalography (50 c.c. air were introduced by suboccipital and 30 c.c. by lumbar puncture): the anteroposterior picture showed very dilated anterior horns, without, however, any abnormal configuration. The cavum septi pellucidi was enormously dilated (fig. 1). Radiograms taken two days later showed that the air had passed from the cavum septi pellucidi to the lateral horns, the 5th ventricle had disappeared and the anterior horns had become considerably wider. The lateral ventricles and the posterior horns were also very much dilated. Quantities of air were present in the subarachnoid spaces especially around the poles and the con-

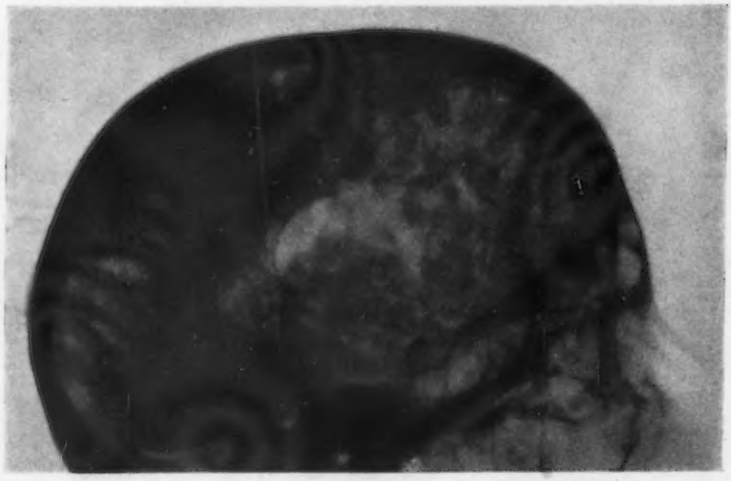

FIG. 2.

vexities of the frontal lobe, and less markedly around the temporal and occipital lobes (fig. 2). The intergyral spaces were unduly wide, and ribbon-like, uniting in cystic confluences. After the suboccipital injection of 2 c.c. of *lipiodol ascendant* the opaque oil settled mostly in the cisterna chiasmatis, a few drops, however, passing into the lateral ventricles.

Course.—During the four weeks of the patient's stay in the hospital her condition became steadily worse. She became unable to find the lavatory, or to get back from there to the ward. Spontaneous grasping occurred on both sides, but more pronouncedly on the right. There was adiadochokinesis in the right arm. The patient's attitude, day by day, was that of an increasing apathy and dementia. She was unable to copy any of *Goldstein-Katz's* figures even if they were left before her. In most instances she wanted to draw her own sketch on the corresponding figure, but gave up the task helplessly after a few meaningless lines. Her failure to

recognize the pictures, or to match them with other objects, demonstrated the patient's incapacity to deal with abstractions. She said spontaneously of the figure:—"This is a triangle, is it not?" This shows that she could recognize the fact that it was a geometric figure but was unable to classify it. Of another linear figure ∧ she said: "Quadrangle, is it not?" Her utterances always betrayed perfect helplessness which was also manifest in the repetition of the questions. In two instances we administered a tablet of benzedrine; thereafter the patient became restless and walked up and down the corridor completely disorientated.

Clinical summary.—The patient presented intellectual deterioration beginning at 52 and progressing during the following five years, characterized by a lack of initiative, apathy, impairment of perception and of the reception and retention of engrams, of the critical faculties and an inability to form abstractions. The neurological findings were: naso-oral and naso-mental reflexes positive, forced grasping on the right side. Encephalogram: enormously distended ventricles, wide intergyral cavities presenting a strip-like aspect with cystic confluences, especially over the frontal region.

Case 2.—A. B., female, aged 50, was under observation in the University Neurological and Mental Hospital, Budapest, from January 29, 1937, to April 23, 1937. *Family history:* Her father died at the age of 75; in the last years of his life he was markedly senile. *Personal history:* during the two years preceding her admission the patient was forgetful; she neglected her household duties, complained that she was not to be trusted with anything . . . "that she was like an idiot."

Neurological examination.—The optic fundi and cranial nerves were normal; the pupils reacted well to direct and consensual light and on accommodation. There was a slight tremor of the eyelids. The tendon, periosteal and superficial reflexes were normal. There were no pathological reflexes and no clonus. There was no grasping, groping, sucking reflex or "Gegenhalten." There were no motor or sensory disturbances.

Mental examination.—The patient understood words well, her attention, however, was often defective. In spontaneous speech she had difficulty in finding the words; in reading long words she hesitated and omitted syllables. In writing the same features were apparent. She was unable to recognize or reproduce numbers of three or more digits. There was no aphasia, agnosia or apraxia. According to her husband, her handwriting had deteriorated. Her behaviour was characterized by a lack of spontaneity. Usually she lay in bed, or sat in one place without stirring. She displayed no interest in her surroundings. Her spontaneous activities were limited to the more necessary actions, such as going out to the lavatory or for her meals. She was apathetic, but open to emotional approaches, liked her home, was glad to see her husband and talked willingly about her children. Her attention was affected; she could not concentrate on a subject even for a few seconds. She was unable to carry out double or triple commands. She could respond to stimuli from without only with great difficulty. Because of the serious defect of attention her ability to receive engrams could not be examined by means of the usual clinical tests. Her reproductive memory was defective but improved on repeated and energetic questioning; indicating a state of pseudodementia. Her orientation in space, on the whole, was retained, while in time she was totally disorientated. Her insight into her condition varied; at times she felt that she was healthy, at other times she complained of forgetfulness.

Physical examination and the laboratory investigations revealed nothing abnormal. In particular the cardiovascular system was intact. The blood pressure was 125/95 mm. The Wassermann test in blood and cerebrospinal fluid was negative, and the colloidal and globulin reactions in the fluid were perfectly normal.

Encephalography.—25 c.c. of air were introduced suboccipitally: the right lateral ventricle was slightly but evenly dilated while the left lateral ventricle, on the whole, was of a normal configuration. The subarachnoid spaces were much dilated over both frontal lobes, especially over the polar and orbital surfaces.

Cerebral arteriography with 25 per cent. thorotrast solution showed conspicuous changes in the configuration of the anterior cerebral artery (fig. 3). Its pericallosal branch showed a changed course from its origin in the upper curve of the carotid syphon. Instead of passing upward and forward in a wide curve corresponding

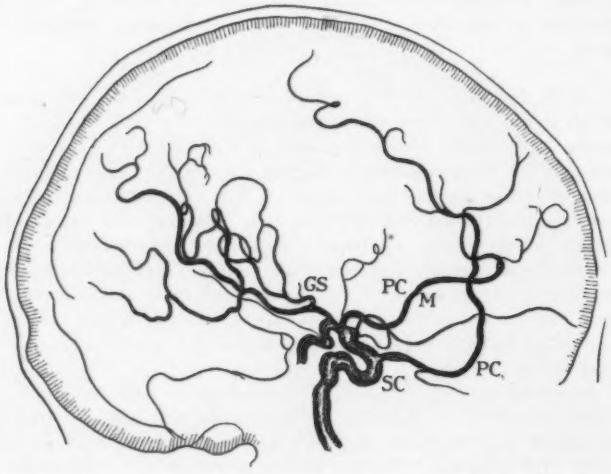

FIG. 3.—GS = Sylvian Group, SC = Carotid Syphon, PCM = Art. Pericallosomarginalis, PC = Art. Pericallosa.

to the convexity of the genu and body of the corpus callosum, it turned up and backward only after having crossed the double projection of the pars orbitalis of the frontal bone. The A. pericallosa marginalis also originated in the upper curve of the carotid syphon, and ran obliquely forward and upward crossing the pericallosal artery in an unusual fashion. It may therefore be assumed that there was a considerable atrophy of the frontal part of the corpus callosum which deprived the anterior cerebral artery of its support and so resulted in undulations in its course instead of the usual spanned arch. The part corresponding with the genu was straight and steep. In the first part of the A. pericallosa marginalis there were deep and sharp breaks due to the severe atrophy of the convolutions and the separation of the sulci. A similar deep and sharp break was to be observed in the external orbitofrontal artery and the perolandic artery and on the prefrontal artery. The topography of the Sylvian group of vessels presented, on the whole, a normal

picture. There were considerable changes in the carotid syphon. The upper curve was obviously compressed and pushed downward, and the final part of the carotid, forming the upper branch, was flattened. This may be explained by the fact that owing to the atrophy of the frontal lobes the subarachnoid spaces became distended and their increased cerebrospinal fluid contents exerted pressure upon the carotid syphon, the more so as the cisterna chiasmatis and the lamina cinerea terminalis shared the increased local pressure.

Brain puncture was carried out by the Neisser-Pollak technique.—Brain cylinders containing the 1st, 2nd and 3rd cellular layers of the frontal cortex were stained by Nissl's method. All the nerve cells were pathological, the majority showing honeycomb-like degeneration. Fatty degeneration and to a lesser extent homogenous sclerosis were revealed by fat stains. The glia participated actively in the process of the demolition of the fats; in the white matter there was an increase of glia. A silver impregnation stain showed small argentophil senile plaques scattered throughout the cortex. There were no Alzheimer's fibrillary changes. Here and there the axons showed evidences of degeneration.

Course.—After the brain puncture there were signs of meningeal irritation with fever, rigidity of the neck, Kernig and Brudzinsky's signs. There followed a rapid deterioration in the patient's condition. Her attention became even more impaired and her answers inadequate; she displayed a demented euphoria. She sang much during the day and laughed stupidly. The neurological findings remained negative.

Clinical summary.—An intellectual disintegration, starting at the age of 48 years, proceeding slowly, characterized by a lack of spontaneity, a grave impairment of the reception of engrams, complete disorientation in time, loss of higher productive intellectual processes, limitation of the mental horizon and of the capacity for attention. The encephalogram showed extensive atrophy of the frontal lobes. Angiographically it was possible to demonstrate atrophy of the frontal region and of the corresponding parts of the corpus callosum.

Case 3.—B. I., aged 61, female, was under observation in the University Neurological and Mental Hospital, Budapest, from November 20, 1937, to July 9, 1938. No *family history* was obtainable. *Personal history*: Climacteric at 48, followed by periods of excitement for two years. At 56 she became gradually more and more restless. This phase was followed in the two years preceding her admission by a gradual lack of spontaneity, disturbance of speech, and depression, later by dementia. Four days before her admission she lost her way in the street.

Neurological examination.—The fundi were normal. The cranial nerves showed no abnormality. The pupils reacted promptly to direct and consensual light, as well as on accommodation, but with a small excursion. Motor symptoms: gait was normal but slightly stooping. The tendon reflexes were increased and the naso-oral and naso-mental reflexes easily elicited. There were no signs of a pyramidal or extra-pyramidal lesion, no tonic neck reflexes, no abnormal postural reflexes, no "Stützreaktion" (extensor thrust), no "*Gegenhalten,*" no grasping or sucking reflexes. Sensation was intact and there was no disorder in any of the special senses.

Mental examination.—The psychological picture was dominated by a grave disturbance of speech. She could not understand questions nor speak spontaneously, although she was capable of phonation. She had also lost her ability

to write, read, repeat after hearing, as well as to copy writing or drawings. She was equally at a loss with written as well as oral direction. Whatever the demand, she wrote when given a pencil a capital B followed by stereotyped illegible lines in the likeness of a signature. At times she could utter a few short words like "Yes" or "No"; the rest of her speech was unintelligible. It must be emphasized that the patient was not mute, for when alone she murmured incomprehensible fragments of words. The only means of communicating with her was by way of

FIG. 4.

gestures. At times she was able to perform required tasks by imitation. She understood the significance of a hand being reached out to her; she could be induced with suitable gestures to undress; she even assisted in attending to the patients. In all her actions there was a conspicuous tendency to perseveration. Movement once begun was continued even when it had become unnecessary. At times she confused different objects and tried to use a comb for a toothbrush. There is justification therefore for diagnosing an ideomotor apraxia. She could repeat songs, or sing quite correctly in unison, pronouncing the text also; how-

ever, she could never repeat the text alone. Her behaviour was quiet and composed. She sat all day quietly, with an utter lack of spontaneity and initiative. Her attention was relatively good as shown by emotional responses and her ability to imitate. She watched her companions and joined them in their occupations. An exact examination of attention, however, was just as impossible as that of perception, memory, intelligence and orientation, because of the great incomprehension of words. Emotionally she was approachable; she was glad to see her relatives, and understood expressions of pleasure and anger. She was unable to solve any of the Herderschee tests for the examination of deaf-mute children. She could not comprehend the simplest tasks.

Physical examination showed nothing abnormal. The cardio-vascular system

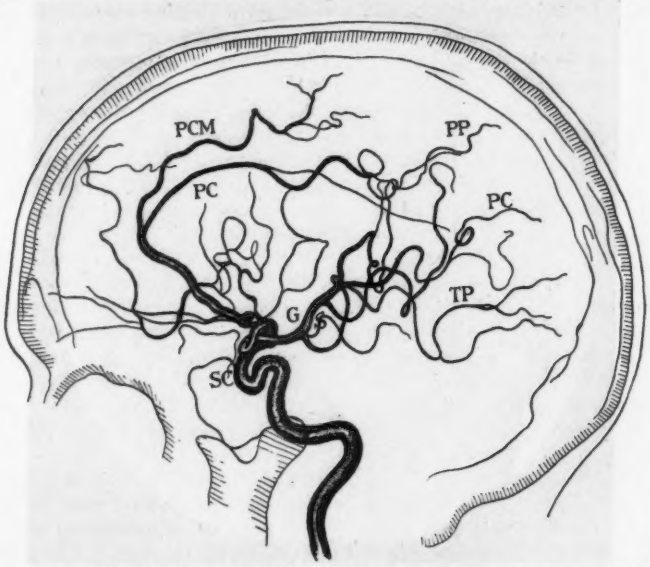

FIG. 5.—GS = Sylvian Group, SC = Carotid Syphon, PCM = Art. Pericallosomarginalis, PC = Art. Pericallosa, PP = Art. Pariet. Post., TP = Art. Temporalis Post.

was intact; the blood pressure 175/80 Hg mm. Wassermann test in the blood and the cerebrospinal fluid was negative, the cell count in the fluid was 5/3, the albumin content 20 mgm.%; chlorides 0·6%; all colloidal reactions normal; globulin reactions negative. The urine was normal.

Encephalography (80 c.c. air suboccipitally, 30 c.c. by lumbar puncture).—The ventricle showed a considerable generalized dilatation (fig. 4). The intergyral cavities of the frontal and temporal and to a lesser extent of the parietal region appeared on account of the extensive atrophy as round or longish, ribbon- or cyst-like formations. Especially conspicuous were two larger cysts formed by confluent small cavities on the lower and lateral part of each frontal lobe, corresponding with the frontal opercula.

Arteriography.—The paracentral and posterior part of the left pericallosal artery was slightly undulating; at the same place the pericallosal marginalis showed sharper angulation (fig. 5). Traces of the same feature were visible on the posterior temporal artery and the so-called artery of the angular gyrus. The wide curve of the right pericallosal artery was interrupted at a right angle. The carotid syphon showed no considerable changes.

Brain puncture by Neisser-Pollack's method.—In material obtained from the frontal region the pyramidal cells of the cortex were either finely vacuolar (honeycomb-like degeneration), or swollen with homogenous sclerosis (dark cell plasm, pyknotic, angular nucleus). At times there were cell-shadows. The glial nuclei

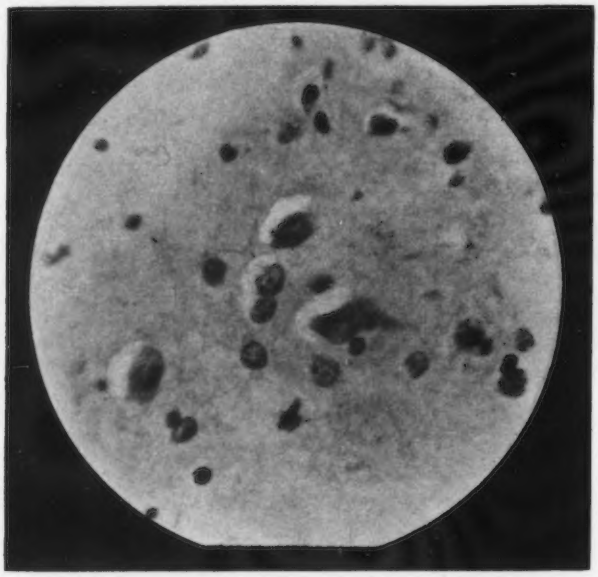

FIG. 6.—*Case 3.* Photomicrograph showing tissue obtained by brain puncture. Nissl's stain; × 585. The nerve cells show the pathological alterations demonstrated on fig. 11. The glial nuclei are light, swollen (active phase).

were mostly light in colour and slighty swollen with hypermetachromatic granules around the nucleus (fig. 6).

Course.—The encephalography was repeated at intervals of four to six weeks with identical quantities of air, the patient tolerating all interventions well. *The large opercular cyst visible in the anteroposterior views became in subsequent pictures not only larger and higher, especially on the left side, but also different in shape, i.e. irregularly elliptical instead of triangular as before.* For a more exact picture of the ventricular system *ventriculography* with simultaneous brain puncture was performed on June 8, 1938. The ventricles were considerably dilated. The anteroposterior views showed an abnormal dilatation of the left anterior horn

(fig. 7). This was still more evident in the lateral views (fig. 8) which also showed an extraordinary dilatation of the frontal horn. This with a steep hump-like outline to the upper limit of the anterior horn produced a strange asymmetrical club or dumb-bell appearance. The apex of this protuberance approached in the direction of the cranium the projection of the lamina vitrea. The centre of the arch was projected on the picture immediately below the upper contour of the smaller right frontal horn. Behind the massa intermedia of the 3rd ventricle there was a defect of filling as thick as a pencil, through the trigonum down to

FIG. 7.

the temporal horn. This defect was formed by the glomus chorioideum. These appearances were to a lesser extent visible in the right lateral ventricle. The postero-anterior picture was in correspondence with these findings. After the ventriculography and the brain puncture the patient developed a subnormal temperature (37·9° C.) with weakness and pronounced meningeal signs. At the same time there was asymbolia for pain. The patient showed no evidence of pain or defensive reactions in spite of the intense meningeal symptoms. Later there was a gradual deterioration; she became totally indifferent, emotionally less approachable; her spontaneous speech became still worse; even her "yes" and "no" disappeared. She was unable to walk; kept her lower extremities

bent at the knee and fell sideways if made to sit up. Even in this condition she was at times able to repeat to some extent texts which were sung to her. The naso-oral and naso-mental reflexes could now too be elicited. There were no other abnormal reflexes or pyramidal signs and no evidence of paresis.

Clinical summary.—A pathological process of five years' duration beginning at the age of 56, characterized by a lack of initiative and spontaneity, a tendency towards imitation (echopraxia), relative emotional and attentive accessibility, grave disturbance of speech (sub-total aphasia), with the ability to repeat refrains ("echomusia"). The naso-oral and naso-mental reflexes well marked. She was unable to pass any of the tests designed for the examination of deaf-mute children.

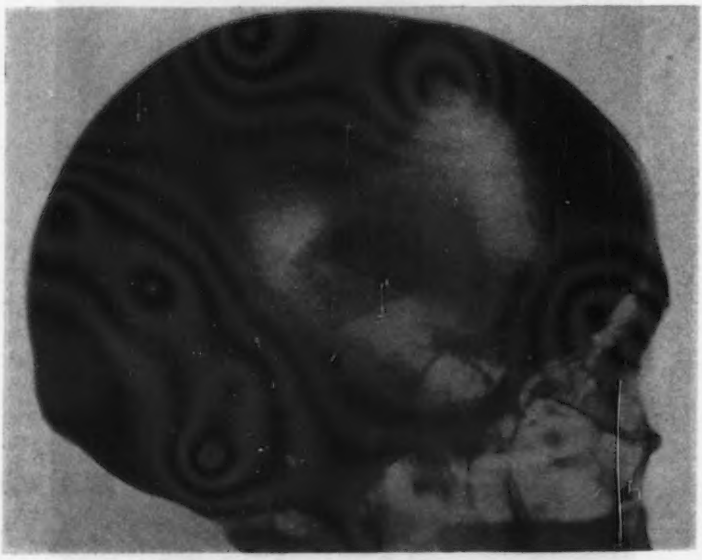

FIG. 8.

The considerable amount of air visible in the encephalographic picture over the fronto-temporal and to a lesser extent over the parietal region demonstrated the severe atrophy of the cerebral cortex. The profound disturbance of speech was associated with the bilateral, but asymmetrical opercular cysts which proved by repeated encephalograms to be growing more and more extensive. The ventriculogram showed a peculiar configuration of the ventricles, being dumb-bell in shape, with the narrow connecting part corresponding to the central part of the lateral ventricle. The anterior and posterior horns were considerably dilated, especially on the left side; the left inferior horn was also increased in size. The arteriogram showed changes indicating cerebral atrophy. The nerve cells in the material obtained by brain puncture showed pathological changes. The meningeal reaction after the brain puncture caused a rapid aggravation of the intellectual deterioration.

Diagnosis.—In the differential diagnosis of the three cases it was important to exclude brain tumour, general paralysis, cerebral arteriosclerosis and senile dementia. All these were eliminated by our clinical and laboratory data.

We should like to consider more carefully the differential diagnosis from Alzheimer's disease, made possible by the following finer clinical symptoms:

In all three cases, in spite of small qualitative and quantitative differences, there was a characteristic form of dementia. In spite of the grave intellectual deterioration, and the serious impairment of the critical faculties, we found in all the three cases an emotional accessibility.

Our first patient was always glad to see her relatives and wanted to go home with them. The attention of the second patient could also be held though only for a while by questions of an emotional content, e.g. regarding her sons. The third patient readily betrayed emotional responses. Both in Case 1 and in Case 3 there was a well-preserved emotional response. These observations are in harmony with those of v. Braunmühl (1934), Stertz (1926) and Schneider (1927), according to whom there does not occur in Pick's disease a complete loss of the mnestic associative functions as in Alzheimer's disease.

As for the general mental attitude, the first two patients, who represented earlier phases of the disease, displayed in a clear fashion the traits said to be characteristic by Goldstein and Katz (1937): "the active abstract attitude in behaviour is lacking, whereas the concrete type of behaviour is relatively well preserved." This was a helpful point in excluding the diagnosis of Alzheimer's disease.

It may be said of the disorder of memory that the most conspicuous element was the almost complete lack of receptive memory. The first patient was unable to repeat the date given a few seconds before; the second was often unable to repeat words immediately. The third patient could not be examined in this respect on account of her aphasia. According to Stertz the cause of this defect is the lack of tenacity of attention, the great distractability of the latter, while according to Goldstein and Katz the cause is to be sought in the inability of the patient to choose between different stimuli. In Case 1 the latter hypothesis seems improbable because the patient also failed if she received no further stimuli in the short interval required for the experiment. With Case 2 the impairment of the receptive memory seemed to be secondary. It was to be explained by the patient's difficulty in applying herself to the actual stimulus. Whatever the cause, it is undeniable that one has to deal with a

grave disturbance of the receptive and retentive memory only, differing from Alzheimer's disease, where the disturbance involves *all* processes of memory. In view of these facts we cannot share Nichol's and Weigner's (1938) opinion. According to these authors it is "not so much memory itself that is lost but rather the use of it in the formation of new ideational material." In our cases, however, there were conspicuous disturbances of receptive and retentive memory, although there was also a "loss of memory as a tool" in Kahn and Thompson's sense.

J. Ley (1935), and Ferraro and Jervis (1936) have suggested other clinical symptoms useful in distinguishing between the two diseases. Of these some are characteristic of Pick's disease, such as anxiety, depression, logoclonia, palilalia and epileptiform seizures. These were lacking in all our three cases. In Case 3 we noted echolalia and echopraxia—said to be characteristic of Pick's disease (Grasse (1934), Ferraro and Jervis (1936)). In all the three cases the patients were apathetic, with expressionless faces; there were no concrete psychotic symptoms; there was no insight into the disease and no pronounced motor disturbances such as paresis or tremor.

From these clinical characteristics we doubtless had to deal with Pick's disease in all three cases. It also indicates that the clinical syndrome as a whole in Kahn and Thompson's (1934) sense may actually be utilized in differential diagnosis.

Encephalo- and arteriography.—We have pointed out elsewhere that though these procedures carefully employed are a great help to the neurologist it would not be desirable were they to attain an undue importance over the clinical findings, thus making the clinical neurological diagnosis a mechanical procedure.

Pneumoencephalic pictures have been utilized by several authors (Lemke (1934), Benedek and Horányi (1937), Nichols and Weigner (1938), and others) for the corroboration of the diagnosis of Pick's atrophy. According to the variants of Pick's disease we may expect either a distension of the anterior horn—in the case of the circumscribed atrophy of the frontal lobe, or a dilatation of the anterior horn, the trigonum and the base of the occipital horn, as in the case of temporal forms. In the isolated lobar destruction of the parietal part we may expect destruction of the cella media, the pars descendens and the vestibular region as well as of the projection of the posterior horn.

(*a*) Our encephalographic pictures showed the symmetrical subarachnoidal air-filling characteristic of Pick's disease: in Case 1 especially over the frontal pole and the convexity, to a lesser extent over the temporal and occipital lobes (fig. 2); in Case 2 on the polar and orbital surfaces of

the frontal lobes; in Case 3 over the frontal and temporal, to a lesser extent over the parietal regions. The air, visible in the form of ribbon-like stripes, spots or small cysts, was localized to certain regions of the brain and *not diffuse* as in Alzheimer's disease (Flügel (1932)).

A special picture is presented by Case 3, where the above mentioned stripes and spots constitute on both sides, but more especially on the left, large cystic formations over the frontal opercular region (fig. 4). This adequately accounts for the grave disturbance of speech. Richter (1918) also found a marked atrophy of Broca's area involving also the orbital gyri. As the encephalography was repeated five times in Case 3 at intervals of four to six weeks, we had a unique opportunity for observing the development of the atrophy of the brain: the opercular cyst appeared, especially on the left side, considerably wider at each subsequent examination. This is in agreement with the aggravation of the aphasia within the last two months of clinical observation.

The ventricular system showed the least changes in Case 2 where there was a uniform distension; in Case 1 the cavum septi pellucidi was visible between the considerably dilated anterior horns (fig. 1). Pictures made two days later no longer showed this formation, and the anterior horns, especially on the left side, were much wider. The other parts of the ventricular system were evenly distended without any peculiarities. An unusual picture was presented by the ventriculograms of Case 3. The ventricular system was greatly dilated. We should like to emphasize the irregularity of this dilatation. Both anterior horns, especially the left, were so enormously distended that they approached within 1 cm. the projection of the lamina vitrea of the calvaria, and downwards the orbital part of the basis of the cranium (fig. 7). The lateral picture showed the anterior horns enormously dilated. The upper contour showed a hump-like protuberance, the centre of the left curve of which was immediately below the upper contour of the smaller right frontal horn. The posterior horn was again much distended, and of a peculiar spherical shape. It passed without any narrowing to the inferior horn which again was enormously wide, especially on the left side (fig. 8). The atrophy was more pronounced on the left. This phenomenon is known to be present in Pick's disease and can be explained by right-handedness. The lateral ventricles accordingly presented a peculiar dumb-bell or club-like shape to be attributed to the relative sparing of the central parts. It should be mentioned that the central part is known to be affected in some cases.

Different parts of the ventricular system present certain slight variations of form though within physiological limits. According to our experience

it is especially the posterior horn that varies. The least variable of the different parts of the lateral ventricles is the anterior horn.

The radiological diagnosis of Pick's disease is therefore not absolute. The use of encephalo- and ventriculography is becoming more and more important with the improvement in technique. In our observations also we obtained data regarding the progressive increase in the atrophy which have not been obtained before during life.

(*b*) The vascular topography may present individual normal variations. Characteristic in this respect is the "formation of knots" as seen in the stereo-angiographic pictures. These facts indicate the necessity of considering the arteriographic findings in conjunction with the radiograms and encephalograms as well as with the clinical findings.

The angioarchitectonic structure may be affected in other ways by atrophic processes of the cerebral parenchyma. The arterial branches may show unusual angulations corresponding with the thinning of the gyri. Instead of a slightly undulating line we may be confronted with a series of sharp bends. This can be observed in our Case 3 (fig. 5), but especially in Case 2 (fig. 3) where there appears a forward and downward deviation of the pericallosal artery and a compression of the carotid syphon. We ascribed these phenomena to an atrophy of the frontal lobes and of the corpus callosum. In a more severe cystic atrophy it is possible that the artery no longer follows the surface of the atrophic gyrus, but remains spanned over the sulcus. At such times the irregular undulations of the arteries are replaced by straight lines or wide arches formed by rigid blood vessels. This can be seen in Case 2 and to a lesser extent in Case 3. A similar appearance was shown in one of our cases of disseminated sclerosis with considerable cortical atrophy where the angiographic features were confirmed at autopsy. In this case the blood vessels were straightened, especially in the territory of the anterior cerebral artery. It was interesting to observe in stereoscopic angiograms that the level of the polygon formed by the pericallosal and the pericallosa-marginalis vessels formed an oblique angle towards the corresponding hemisphere on account of the atrophy of the cortex. In other cases the arterial systems deprived of their support may be dislocated and form unusual crossings as in Case 3 (fig. 5). The destruction of the nerve substance, the shrinkage of the supporting tissues and the regressive hyaline and fibrotic changes in the walls of the blood-vessels, produced in our cases of general paralysis a fairly characteristic though scarcely a pathognomonic stereo-arteriographic picture: rigidity of the arterial stems, discontinuity of the terminal branches and an arterial network devoid of detail. In a case of amyotrophic lateral sclerosis with

bulbar involvement there were psychological symptoms suggesting extensive cortical atrophy. Our angiograms here too showed the well-known changes, the sharp breaks and saddle-like hollows in the pericallosal artery, the compression of the right carotid syphon, the conspicuous thinning of the pericallosal-marginalis and of Duret's internal frontal arteries.

Neisser-Pollack's internal brain puncture.—Cylinders obtained by brain puncture in Cases 2 and 3 showed extensive and marked changes in the frontal cortex: mostly honeycomb-like degeneration with evidence in appropriately stained specimens of fatty degeneration, and to a lesser extent homogeneous sclerosis (fig. 6). The glia took an active part in the process of fat dissolution. The glial nuclei were light and were surrounded by hyperchromic granules. In Case 2 it was possible to demonstrate by the Bielschowsky impregnation method small incipient senile plaques consisting of amorphous argentophil areas with no concentric or radial structure. There were no Alzheimer fibrillary changes. The axons showed at certain places degenerative changes both in the cortex and in the medullary substance. These changes afforded also a histological proof of the severe affection of the cerebral region in question. In the literature of the subject only in Lemke's case was the diagnosis confirmed by brain puncture.

It is noteworthy that in both cases the brain puncture was followed by a meningeal reaction which in its turn resulted in an increased activity of the fundamental process.

Neurological changes.—In Case 1 there was a somewhat sluggish reaction of the pupils, senile changes in the fundus, grasping and groping (more on the right side) which later became more obvious during the month while the patient was under observation. This frontal symptom is rare, according to Schneider (1927), and occurs only in slowly progressive cases. In Case 1 and Case 3 there was a very pronounced naso-oral and naso-mental reflex; these have not been mentioned before in the literature of Pick's disease.

Schmitz and Meyer (1933) have described a reaction which consists of opening the mouth when any object is held in front of it. Neither this, nor swallowing, licking, chewing or sucking reflexes were observed in our cases.

In all the three cases the frontal syndrome was represented above all by mental symptoms, by a lack of impetus and of spontaneity, and by disturbances of volitional initiative.

The speech of our second patient showed a change inasmuch as the association of ideas with the corresponding names was affected; the "symbolic function" (Head) was disturbed in its motor aspect.

The disturbance of speech in Case 3 was a total aphasia with the difference that though the patient failed—as in the other tests—in the repetition of phrases, she could sing a text faultlessly with the examining physician. This symptom occurs chiefly in motor aphasia. The only observation similar to ours has been made by Schmitz and Meyer, with the difference that their patient did not speak for weeks. *We propose to call the symptom echomusia.* In its causation a certain rôle may be played by the emotional accessibility of the patient, for, as the patient became emotionally duller the echomusia also became less evident. In this case we also found echolalia and echopraxia, at times palilalia (Grasse).

In Case 1 as in Rosenfeld (1909) and Heilbronner's (1900) case, there were no disturbances of speech.

Apraxia, agraphia, alexia, acalculia were absent in Cases 1 and 2, the minor disorders of action, writing, reading and counting being due to the disturbances of higher functions. The second patient, for instance, could read long words only by scanning each syllable, starting again and again; she was unable to write down numbers of more than one digit because of the disturbance of receptive memory.

In all the cases the tonic neck reflexes, the postural reflexes, Magnus' supporting reaction, disturbance of standing and gait were absent. In Case 3, during the mental deterioration following the brain puncture and ventriculography, total astasia and abasia appeared and lasted for four weeks, although the meningeal symptoms cleared up earlier, and there were no pyramidal symptoms. No extra-pyramidal symptoms were observed differently from van Bogaert's case. We may mention here the opinion of Critchley (1931) that some of the neurological symptoms in elderly patients are due to lesions of the basal ganglia.

Heredity. Gans (1922), and Onari and Spatz (1926) considered the possibility of the phylo- and ontogenetically youngest and therefore most vulnerable frontal regions, especially Brodmann's areas 43 and 46, being first involved in the atrophy. Later Richter (1918) emphasized the heredodegenerative character of the illness. There have since been extensive investigations regarding the genetic circumstances of the cases. The familial character of the disease is proved by data established by Fischer (1910, 1911), Benders (1915), Grünthal (1930), Haškovec (1934), v. Braunmühl and Leonhard (1934). Schmitz and Meyer's family tree also seems to prove the hereditary character of the disease. In opposition to these authors Moyano (1932) has recently denied the hereditary character of the affection. Only in one of Löwenberg's four cases were there hereditary trends. Guillain, Bertrand and Mollaret (1934) put forward the

possibility of an infective origin. Ferraro and Jervis suggested a vascular origin (" we assume that vasomotor factors play a rôle in the pathogenesis of Pick's disease ").

In Case 1 there is indubitably a significant family history. The patient's father died at the age of 37 of a psychosis. His death is said to have been preceded by two fits of apoplexy. It is possible that the father was already suffering from Pick's disease and the fits of apoplexy were Stertz's (1926) seizures. Her mother also died of psychosis, at the age of 60. Nothing is known of her condition except that it was some kind of depression. In Case 2 there is a suspicion of the patient's father having died at an advanced age of senile dementia. Both in Cases 2 and 3, however, there are no clear heredofamilial data.

We think, from the data published in the literature, as well as from our own observations, the importance of heredofamilial factors may be taken as established.

Summary.

(1) Three cases of Pick's disease all presented positive encephalographic findings. In two cases confirmatory evidence was obtained by brain puncture.

(2) The encephalogram showed in one case the 5th ventricle, in another extensive opercular cysts on both sides. A progressive increase in the size of these cysts was demonstrated by pictures taken successively at intervals of four to six weeks: the progress of the disease was thus encephalographically demonstrated.

(3) Cerebral angiograms showed changes attributable to the atrophy, such as compression of the carotid syphon, the curving forward and downward of the pericallosal artery, deep and sharp bends in several arterial branches. All these were more pronounced in Case 2 than in Case 3.

(4) Brain puncture demonstrated a severe degeneration of the frontal cells and axons, an activity of the glia, and in Case 2 incipient senile plaques.

(5) The ventriculogram of Case 3 presented a very unusual picture. The projection of the frontal horns of the lateral ventricles became enormously bulging, especially on the left side, thus giving the ventricular system a peculiar dumb-bell or club-like appearance.

(6) According to Schneider's (1927) classification, Cases 1 and 2 were transitional forms between Stage II and III, while Case 3 represented an early form of Stage III.

(7) On the basis of these three cases it may be asserted that the clinical-syndrome in itself is sufficient for the differential diagnosis of the disease.

(8) Of the clinical signs the following are noteworthy: In Case 1 the senile changes in the fundus and the grasping and groping; in Cases 1 and 3 the naso-oral and naso-mental reflexes; in Case 2 the transcortical aphasia, in Case 3 an almost complete aphasia. In the last case there were echolalia and echopraxia as well as a rare symptom we have called echomusia.

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Notices of Recent Publications.

Beitrag zur Kenntnis sklerosierender Entmarkungsprozesse im Gehirn, mit besonderer Berucksichtigung der diffusen Sklerose. By Larus Einarson *und* Axel V. Neel. Copenhagen: Einar Munksgaard. 1938. Pp. 160. Price Kr. 7.

This monograph is an attempt to classify the many cases of diffuse sclerosis of the brain and of Schilder's disease which have been published in the literature in the hope that such a classification might shed some light on the ætiology of the different groups. The difficulties surrounding this essay are obvious enough; not the least is the fact that many cases, which are published as isolated instances of the disease, have been shown by later observations to be familial. And there must be many other cases in which, for one reason or another, the familial nature of the disease is unrecognized.

Further, in interpreting the histological observations of various authors, their methods of examination and various other individual factors must be assessed. For example, the metachromatic prelipoids on which certain authors have laid emphasis may be invisible or almost so in sections stained by Weigert-Pal or hæmatoxylin-eosin methods. The authors have indeed recognized this difficulty as well as that inherent in the variations of stress which different authors place on different aspects of the disease.

On the basis of their survey of the literature and of their personal observations the authors classify diffuse sclerosis under:—

(1) The glioblastomatous form; (2) the exogenous inflammatory form or *leuco-encephalitis diffusa;* (3) the non-familial degenerative form; (4) the heredo-degenerative form or *leuco-encephalopathia progressiva hereditaria diffusa;* and (5) Balo's concentric sclerosis. Their third type is subdivided into (*a*) cases with mucoid degeneration of the oligodendroglia, and (*b*) cases which are characterized by the accumulation of metachromatic prelipoids in and round the demyelinated areas. Their fourth type is also subdivided into (*a*) the acute infantile type of Krabbe. (*b*) The subacute juvenile type of Scholz. (*c*) The adult type of Ferraro, and (*d*) the chronic type (infantile, late infantile and juvenile) which includes cases resembling the family described by Pelizaeus and Merzbacher.

For the most part this classification is acceptable enough. There are, however, some who consider that Balo's concentric type of demyelination lies nearer to disseminated than diffuse sclerosis. Nor is the blastomatous form of the disease generally accepted. The demyelinating effects of infiltration or pressure by a tumour, or of the œdema to which it may give rise, seem indeed to have been minimized or neglected by many of the authors who have described such cases, and it is therefore dangerous to accept their reports in an uncritical manner. Whether or not a transition form exists between tumour and diffuse sclerosis, linking the disease to tuberous sclerosis as the authors claim, is therefore doubtful.

The authors put forward many suggestions as to ætiology, most of which are

old and are not supported by any stronger evidence than has been put forward in the past. The relationship of diffuse sclerosis in the human to cage paralysis in monkeys is lightly touched on, but no mention is made of "sway back" in lambs, which seems to be a closer and more fruitful analogy. The only new causative factor suggested is an insufficiency of vitamin E. This has been shown by Einarson to have some effect both on the nervous system and the musculature, and, on the basis of the more or less localized muscular wasting which often occurs in diffuse sclerosis, is put forward as a possible factor. No evidence is, however, advanced as to whether the muscular wasting is primary or is secondary to disease of the brain.

Taken as a whole, the monograph does little to increase our knowledge of diffuse sclerosis, although the new case records, especially Case I, are interesting.

Clinical Examination of the Nervous System. By G. H. MONRAD-KROHN. Seventh Edition. London: Lewis and Co. 1938. Price 8s. 6d.

The appearance of the seventh edition of this useful handbook indicates its continued popularity. The section dealing with ventriculography has been amplified and new radiograms provided. In general its plan and contents remain as before.

This work has perhaps not altogether escaped the dangers that beset the endeavour to keep successive editions up to date. The gradual accumulation of new matter tends to blur the original clarity and to overload the framework of the book, as well as to swell its bulk unnecessarily. There comes a time when sections thus amplified need to be recast. Only thus can obsolete and redundant matter be eliminated.

The necessity for such drastic recasting is well seen in the chapters dealing with the reflexes. For example, the student seeking to get information about the extensor type of plantar response: its receptive field under differing conditions, its motor field of response, its relation to the flexion reflex, and its behaviour in the extended and flexed forms of paraplegia no longer finds a continuous and coherent account. The two forms of paraplegia mentioned also need a more adequate description and interpretation than they receive.

It is probable that future revision on these lines will again bring the book to that smaller original compass, the disappearance of which the author now deplores.

Comparative Anatomy and Physio-Pathology of the Autonomic Hypothalamic Centres. By A. A. BOON. Acta Psychiatrica et Neurologica, Supplementum XVIII. Haarlem: De Erven F. Bohn. 1938.

This timely and critical monograph sums up the present state of knowledge of its subject. The author concludes that important as is the hypothalamus in the regulation of vegetative and endocrine functions, its influence may be exaggerated. He cites the clinical observation that considerable lesions may be found in this structure in the absence of noteworthy vegetative disturbances. The bulbar and spinal vegetative centres may, up to a point, compensate for any loss of function the hypothalamus may suffer. On the other hand some hypophyseal and heat-regulating activities are strongly influenced by the hypothalamus, and cortical and striatal influences mediated by pathways from these regions to the bulbar and spinal centres have synapses in the hypothalamus.

Studies on Pain Conduction in the Trigeminal Nerve. By O. Sjöqvist. Acta Psychiatrica et Neurologica. Supplementum XVII. Helsingfors: Mercators Tryckeri. 1938.

The studies recorded in this monograph had as their starting point the practical end of devising a surgical means of abolishing the pain of trigeminal neuralgia without at the same time rendering face and cornea anæsthetic. Dandy had claimed that division of the posterior and inferior fibres of the 5th nerve sensory root near its point of emergence from the pons, produces a selective loss of pain sensibility in the face, but the observation had not been confirmed. Sjöqvist therefore undertook an anatomical study of the distribution of pain conducting fibres within the peripheral portion of the sensory root and also within its intramedullary and spinal portions. Starting with the assumption, for which he relates the relevant anatomical and physiological evidence, that the pain conducting fibres are the smallest, not exceeding 3 μ in diameter in paraffin sections, he traces their course within the central and peripheral portions of the sensory root. This process he speaks of as "fibre analysis." No qualitative grouping of pain fibres could be discovered in the peripheral sensory root of man, of a kind likely to make possible a dissociated anæsthesia by partial root section. But in the bulbospinal portion of the 5th nerve (in *Macacus rhesus* as well as in human material) the smallest fibres predominate, and section of this tract in human subjects of trigeminal neuralgia produced complete pain and temperature sense loss on the affected half of the face.

On the basis of this observation the operation of bulbospinal section for trigeminal neuralgia has been devised. The monograph contains full technical details of the operation, and records an admirably planned investigation with valuable practical results.

Theories of Sensation. By A. F. Rawdon-Smith. Cambridge University Press. 1938. Pp. 120. Price 10s. 6d.

The author gives the present state of knowledge and opinion on the functions of vision and audition, with special reference to the capacity to discriminate differences of amplitude and frequency in light and sound. This discrimination is of fundamental importance and its study throws light upon the wider problems of sensation. The electro-physiological researches of Adrian and his co-workers have extended our means of investigation in this field, and the bearings and promise of this line of research are fully discussed.

The Form and Functions of the Central Nervous System. By F. Tilney and H. A. Riley. London: H. K. Lewis and Co. Third Edition 1938. Pp. 789 and 600 figures. Price 50s. net.

When in 1921 the first edition of this work was noticed in these pages, the hope was expressed that later editions might contain a more adequate account of the physiology of the nervous system, and a terminology less luxuriant. These hopes have not been realized, and the present edition differs in no essential features from its predecessors. The name of Dejerine continues to be wrongly accented,

and some of the figures to be attributed to the wrong authors, or not to have their source acknowledged at all. Thus figures 480 and 481 appear to be reproductions of Spalteholz's figures 710 and 711, while figure 397 attributed to Dejerine appears to be Spalteholz's figure 704. Errors of this order should not have survived into the third edition of a book.

But what is more important is the almost complete absence of mention of some of the major advances in the physiology of the nervous system of the past quarter of a century. The name of Magnus finds no mention and his researches and those of his school are unrepresented.

Where physiological functions are discussed the style is too often that of fifty years ago, when elaborate periphrasis and reiteration in vague abstract terms were the only available substitute for the physiological knowledge that was not then acquired. Thus the function of the Betz cells of the cortex is said to be to "transmit a part of the skilled motion formulæ." To speak of a cell transmitting a formula is not to use the language of science, nor indeed any language that has discoverable meaning, for cells do not transmit abstractions.

The discussion of cerebellar physiology is a striking example of a lavish use of abstract names that have no discoverable referents. Even where such a familiar phenomenon as Babinski's toe response is mentioned, no interpretation of it in terms of normal function is given, though the response has a considerable physiological interest.

It may be doubted, also, whether within the term "functions" of the nervous system a description of clinical syndromes of local lesions can be reasonably included. For these syndromes represent symptoms of lesions, and these are not the same as normal functions.

Nevertheless, despite these criticisms, the appearance of the third edition of this book indicates that in its present form it has been found of value to a number of readers, though of what category cannot easily be surmised, and if it is to continue in this form, a change of title that would warn the reader not to expect a statement of modern neurophysiology within its covers seems indicated.

Cranio-Cerebral Injuries. By DONALD MUNRO. London: Oxford University Press. 1939. Pp. 393. Figs. 62. Price 21s.

Within the past twenty years the subject of intracranial tumour has dominated the literature of cranio-cerebral surgery in a measure out of all proportion to its importance. The books and original papers devoted to it are innumerable and ever increasing. They have been very fruitful in some respects. Thus they have shown the importance of a pathological diagnosis as an essential preliminary to operation, and they have recorded many new localizing symptom-complexes and have thus added a much-needed precision to diagnosis. Nevertheless, despite the ambitious claims sometimes made for their surgical treatment, it may not unjustly be said that intracranial tumours remain the forlorn hope of surgery, and, since the glioma and the secondary carcinoma together make up about half the total of intracranial tumours, they must of necessity remain so.

On the other hand the surgery of cranio-cerebral injuries is very inadequately represented in the literature of cranio-cerebral surgery, and this in spite of its manifestly greater importance than the surgery of tumours. Such injuries are

extremely common and are on the increase. The author points out that in the United States there were 112,000 such cases in 1932. Further, as the author also rightly observes, their treatment is essentially a problem for the general surgeon. For these two reasons alone an authoritative and comprehensive account of their symptomatology and treatment is a crying need. Moreover, since the prognosis in adequately treated cranio-cerebral injuries is a vastly more hopeful affair than that of intracranial tumours, however skilfully these may be dealt with, the practical importance of a wide diffusion of knowledge concerning these injuries is clear.

This need the author has met in a wholly admirable manner in the book now under review. He has considered his problem as a whole, and from the points of view of everyone who may be called upon to deal with it, from the doctor who renders first aid at the scene of the injury to the surgeon who deals with the case in the "traumatic clinic." The requirements of treatment at each stage are fully described as also are the necessary diagnostic procedures.

The book is a complete manual of its subject and should be carefully studied by all who may be called upon to deal with head injuries. Its author has placed his professional colleagues under a heavy debt of gratitude to him for thus putting at their disposal so clearly and so judicially the fruits of his large experience.

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